

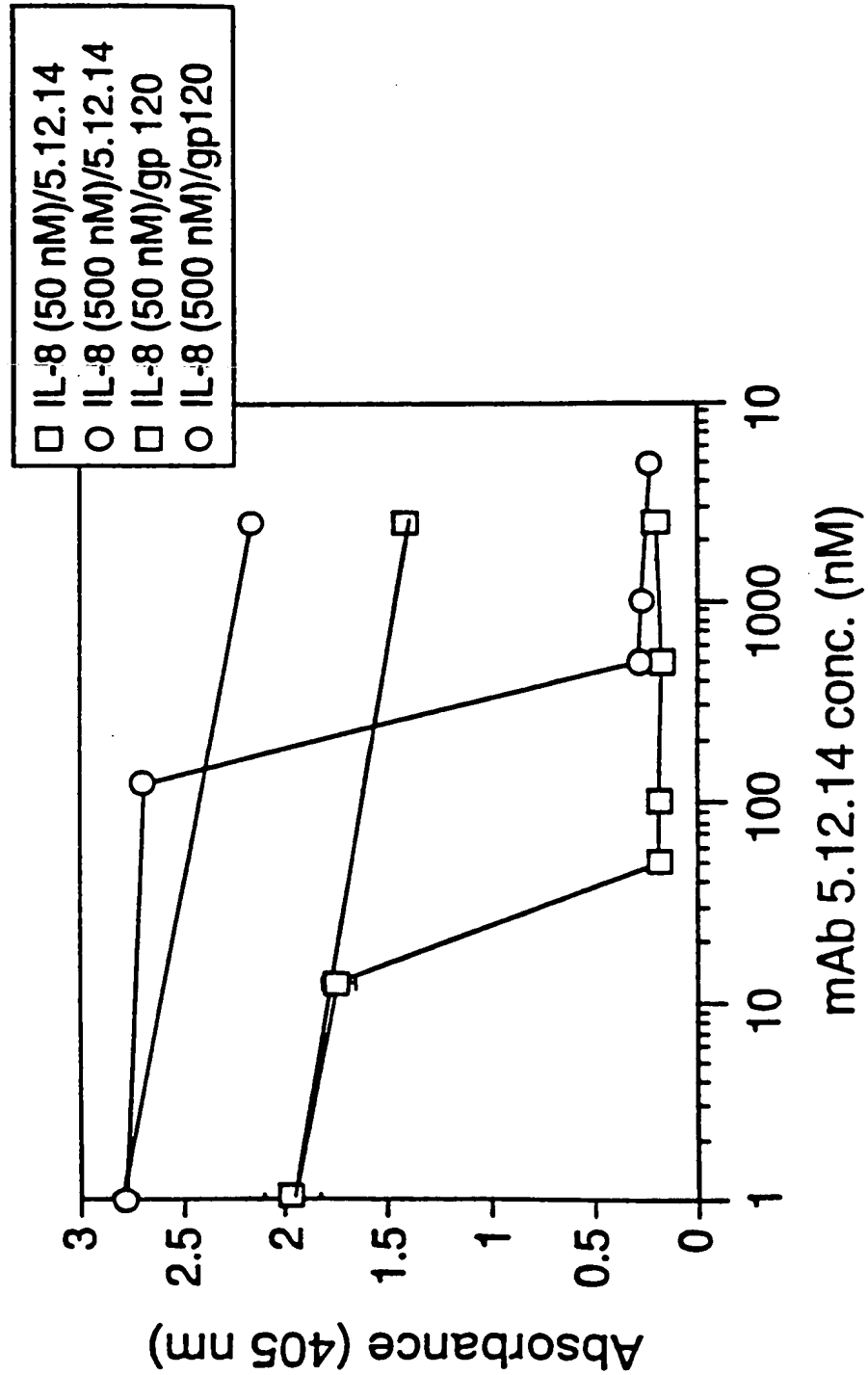


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

FIG. 1



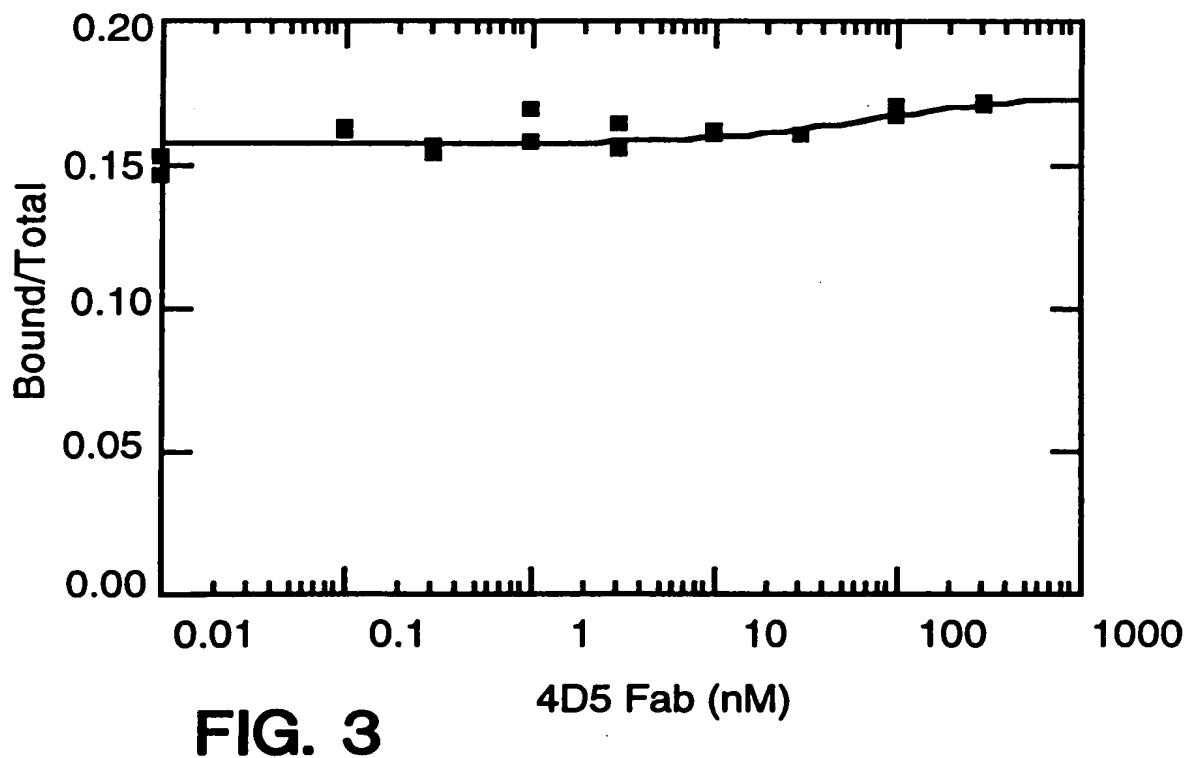
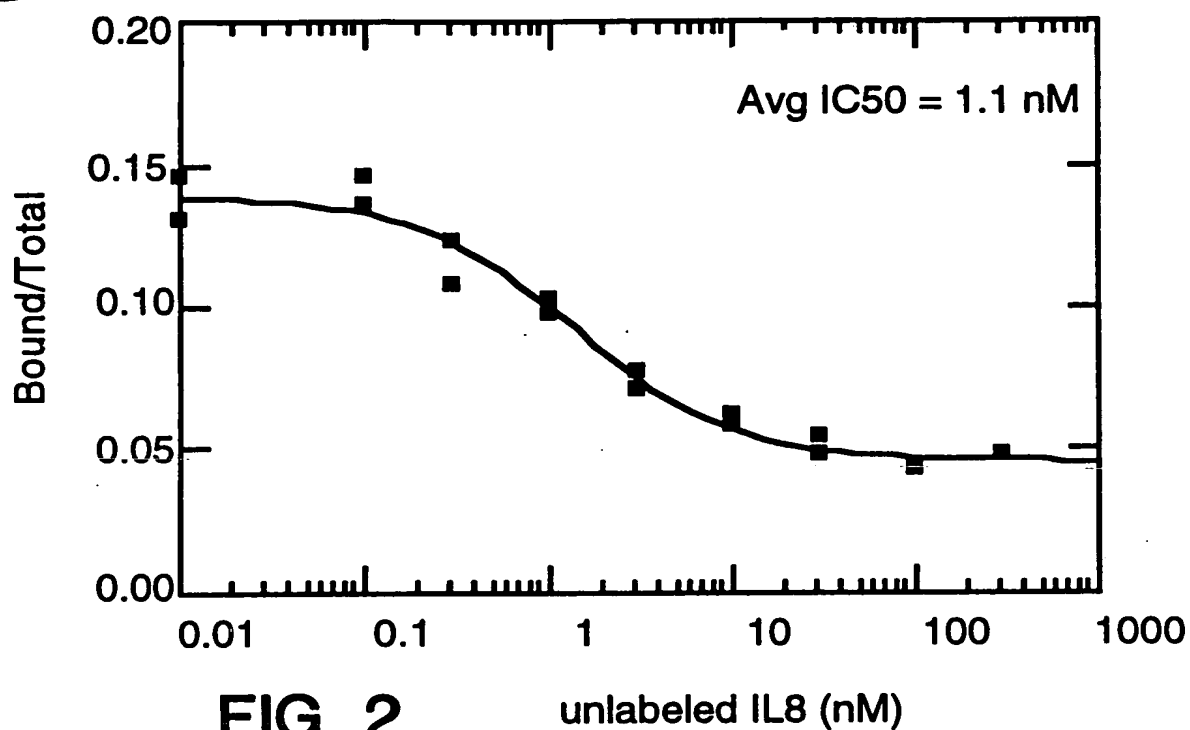


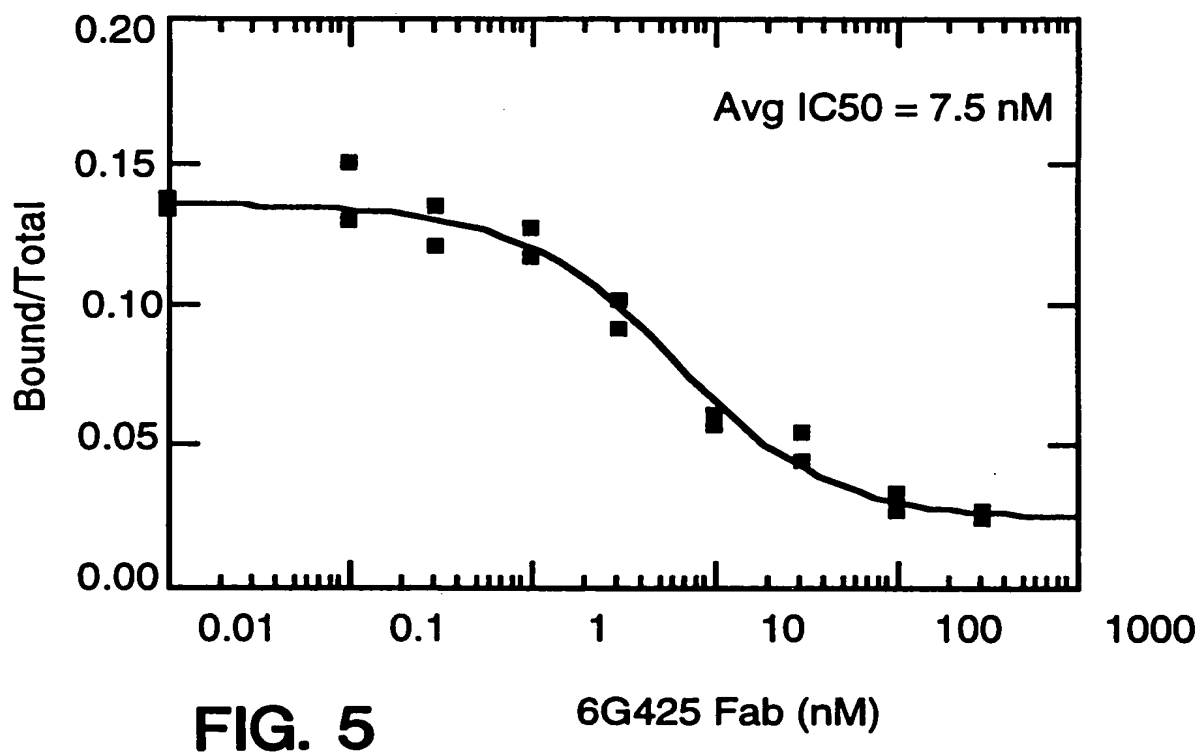
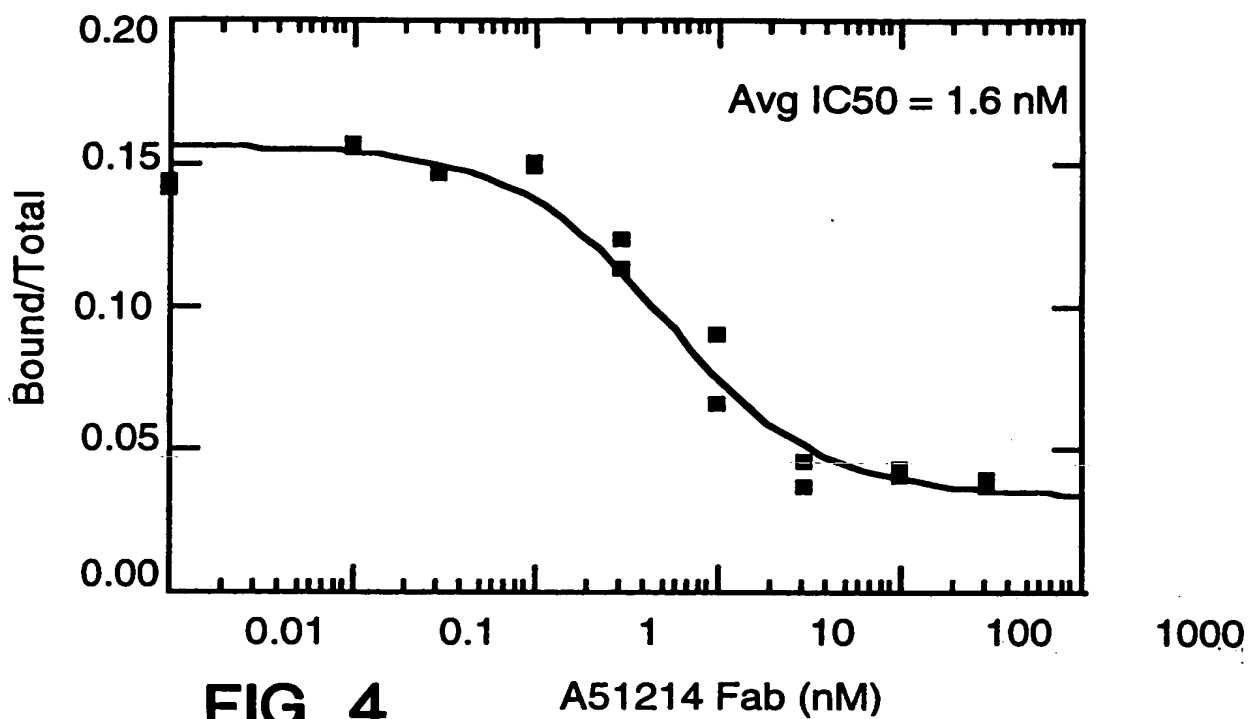
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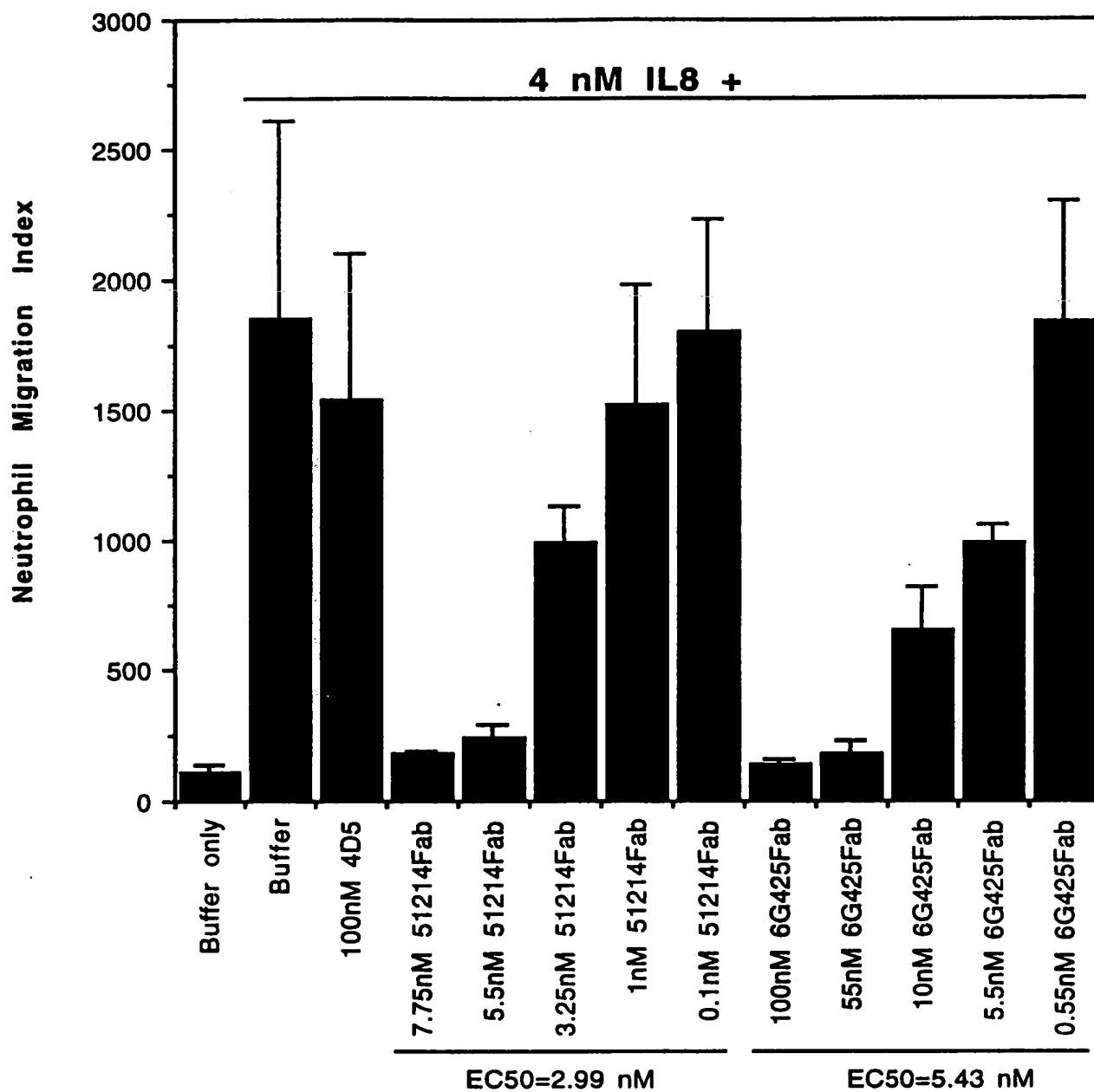


FIG. 6



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
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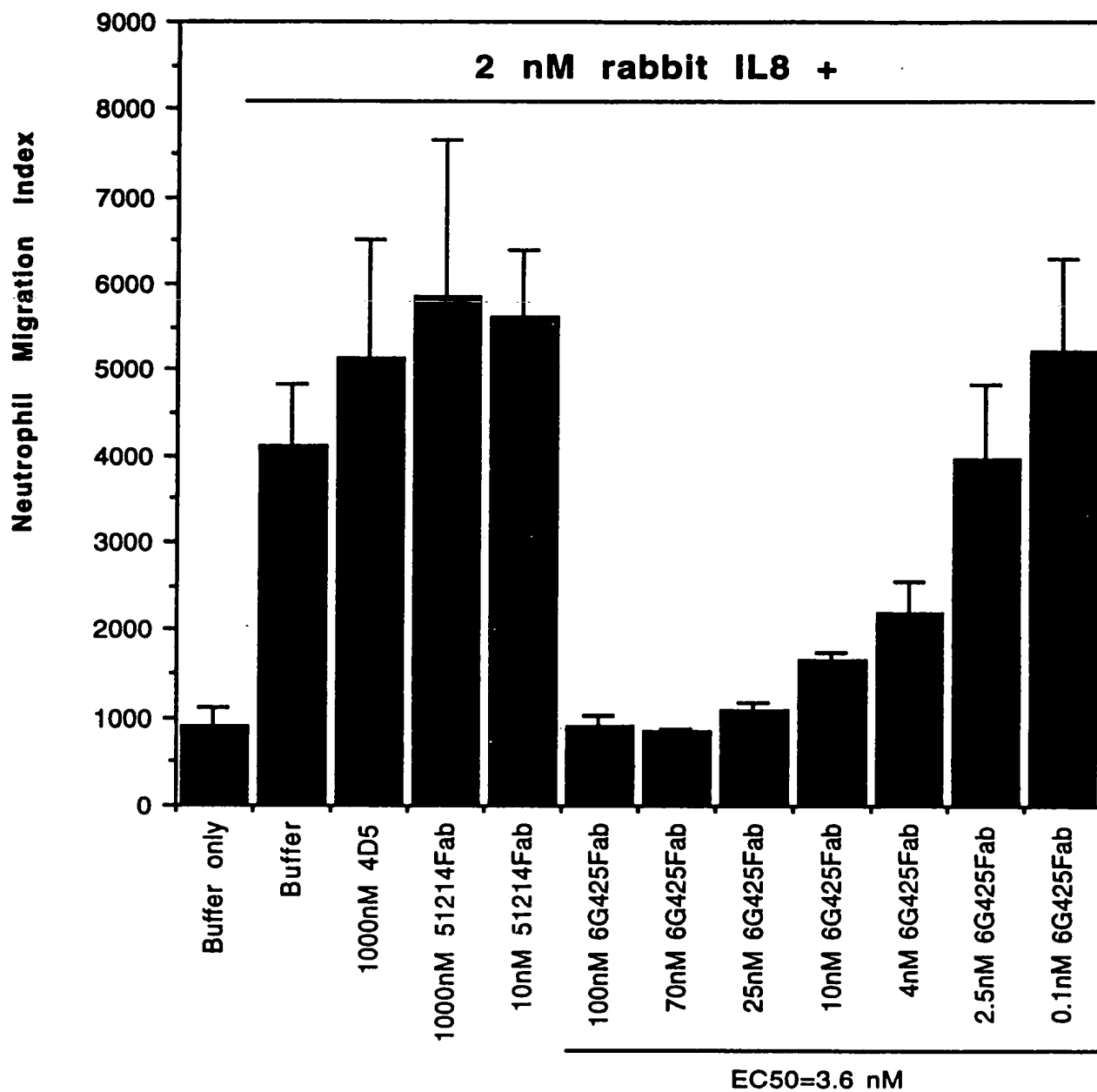


FIG. 7

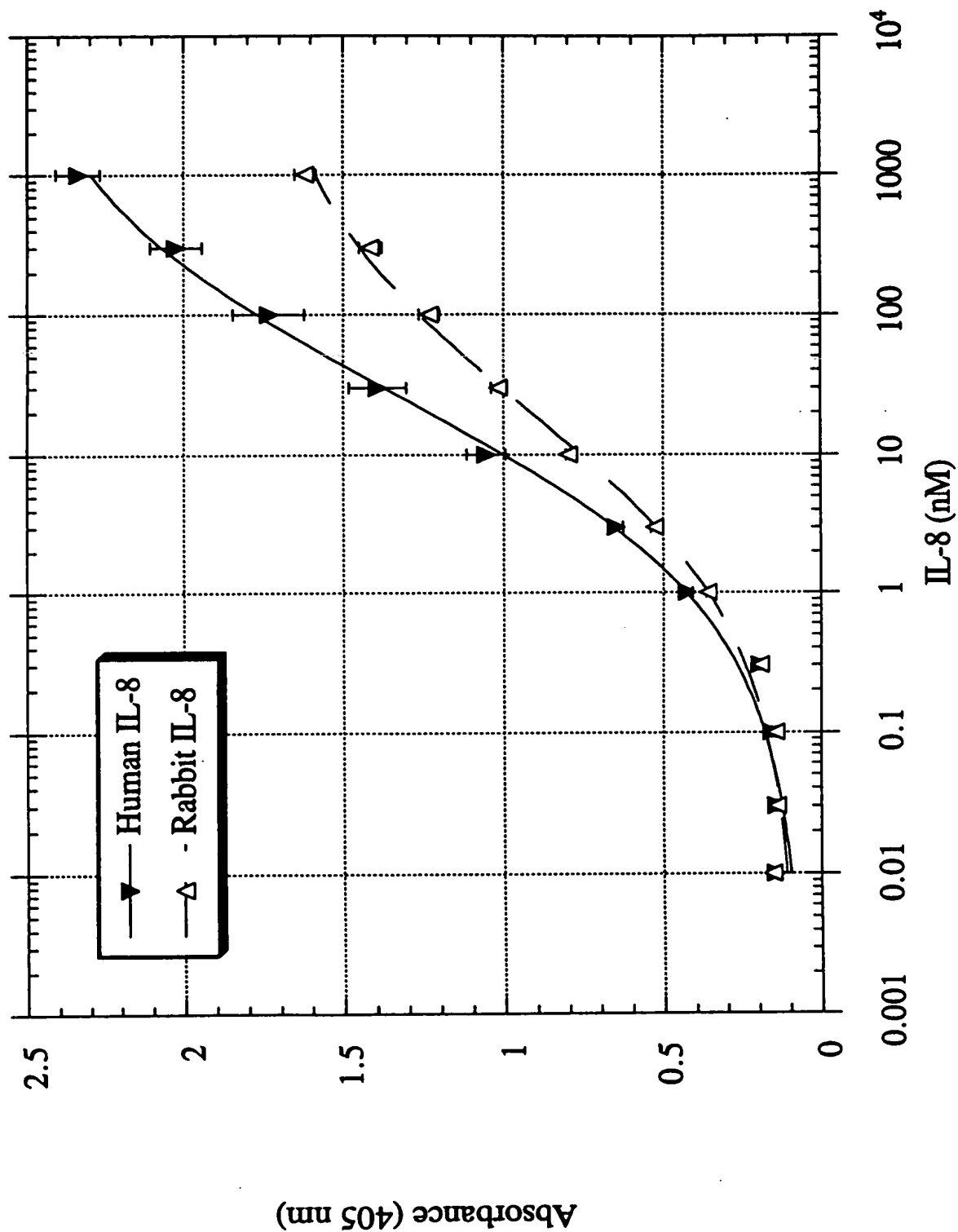


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FIG. 8



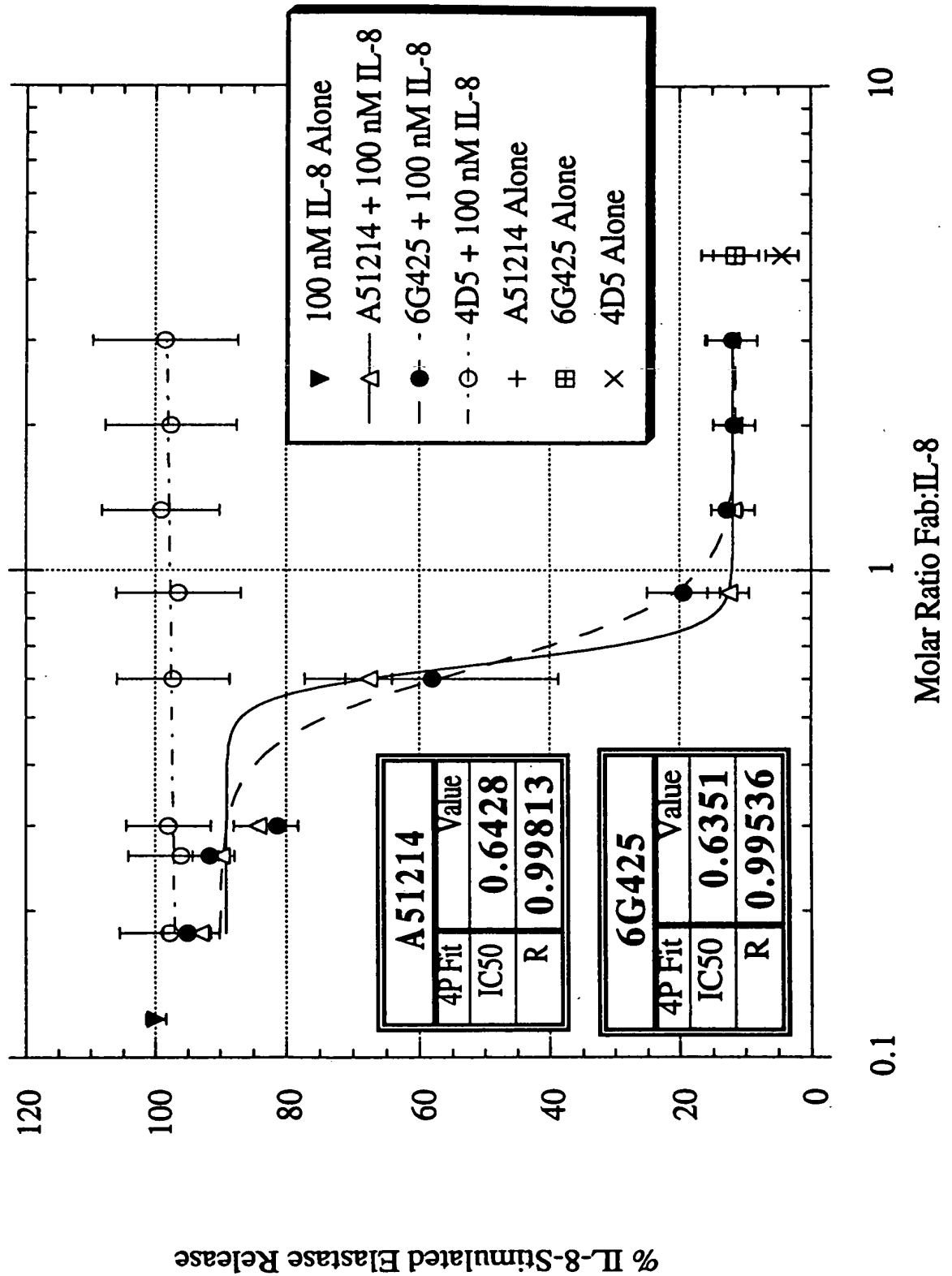


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FIG. 9



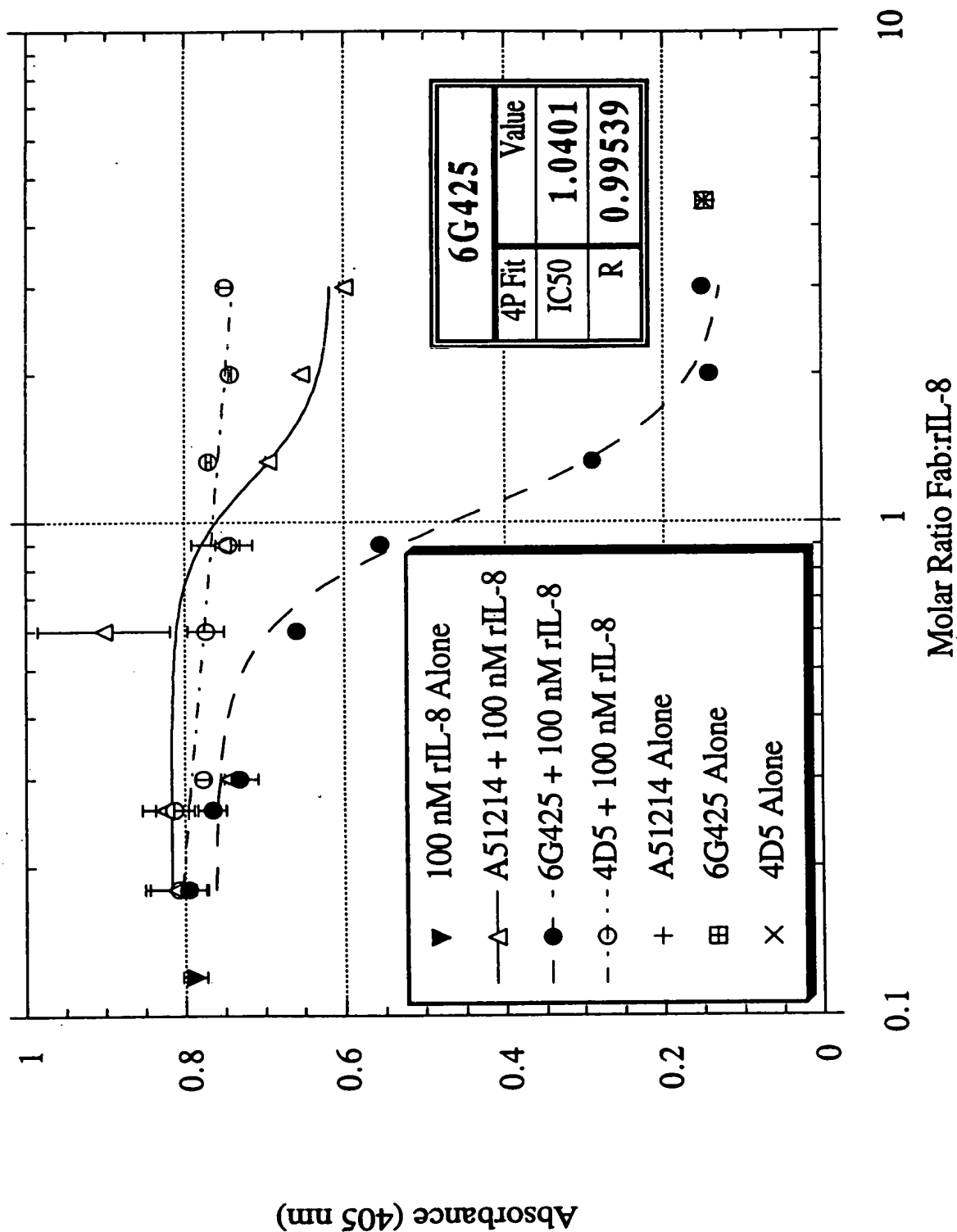


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FIG. 10





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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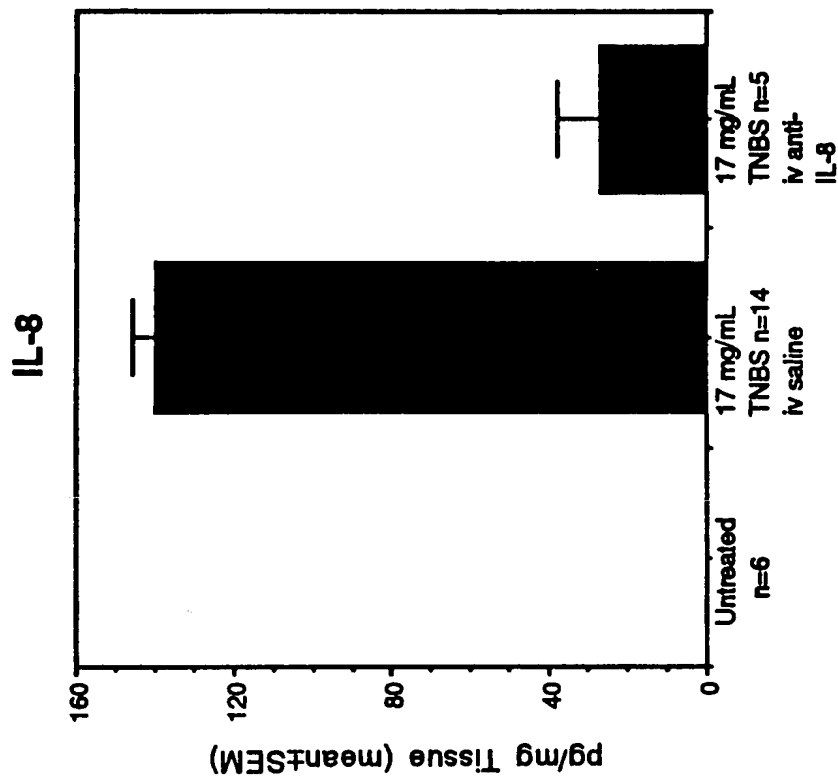


FIG. 11B

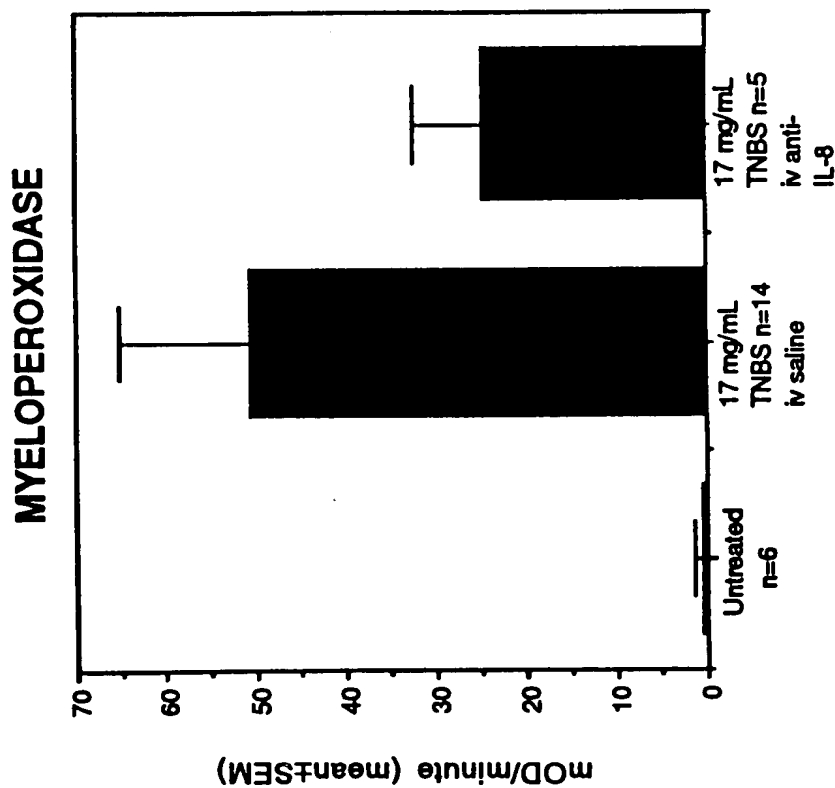


FIG. 11A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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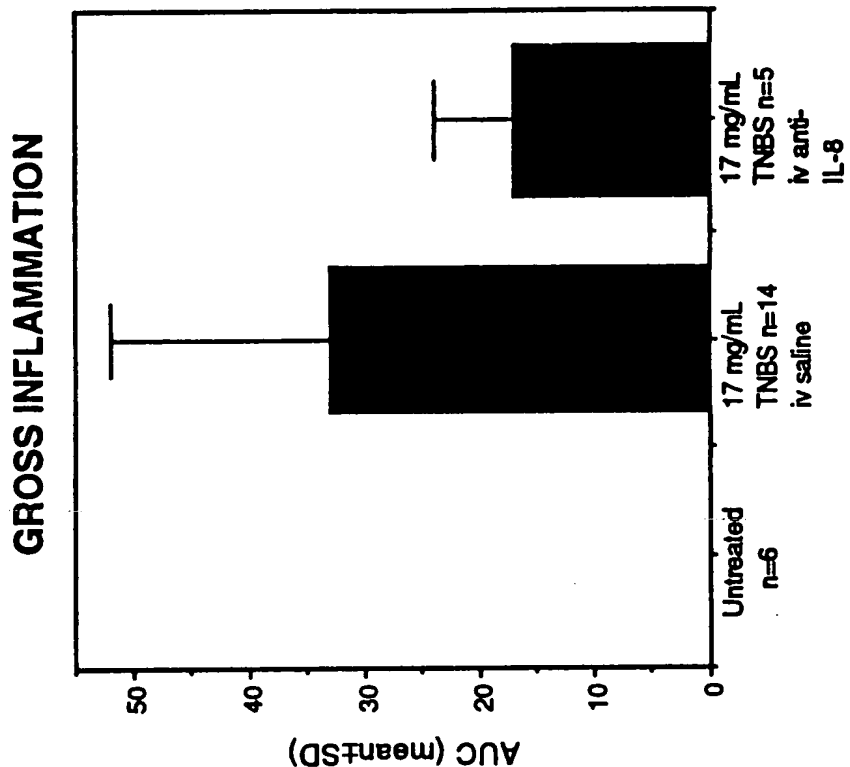


FIG. 11D

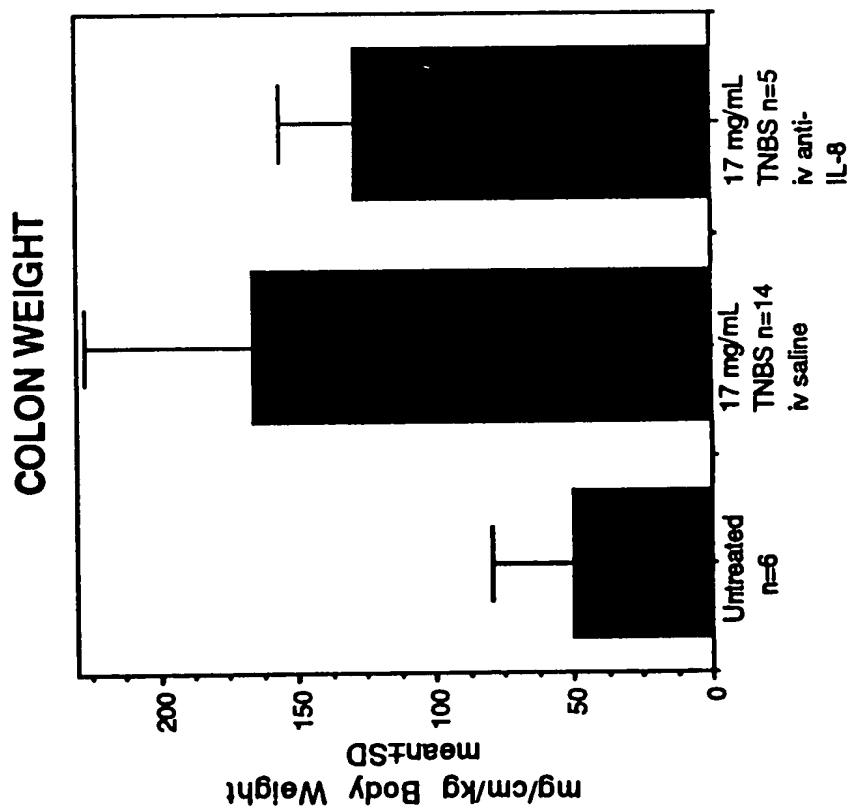


FIG. 11C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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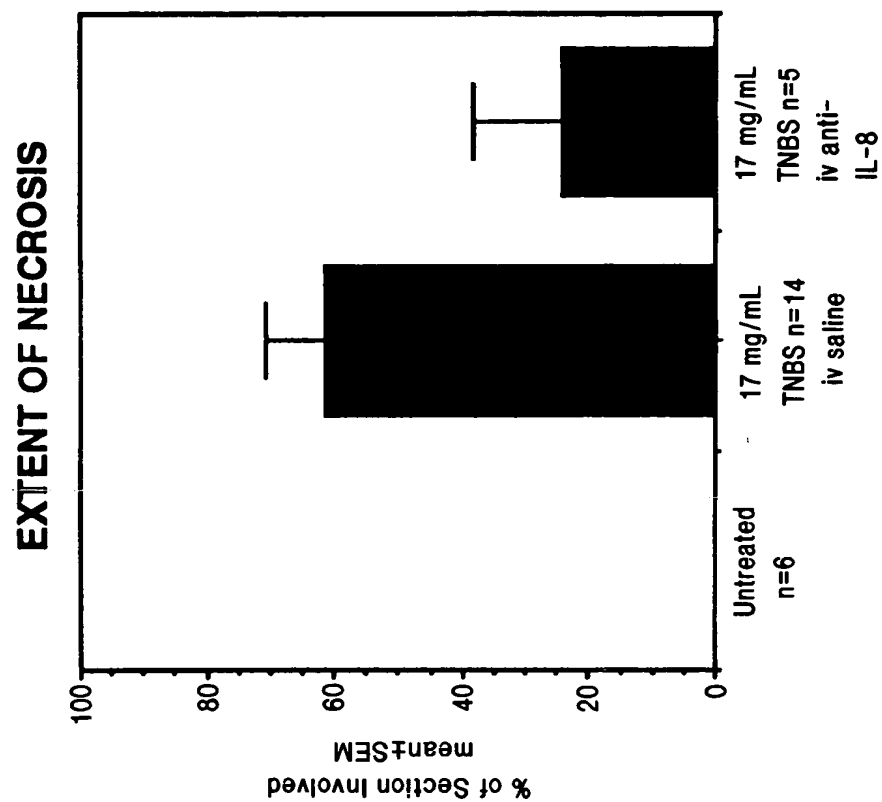


FIG. 11F

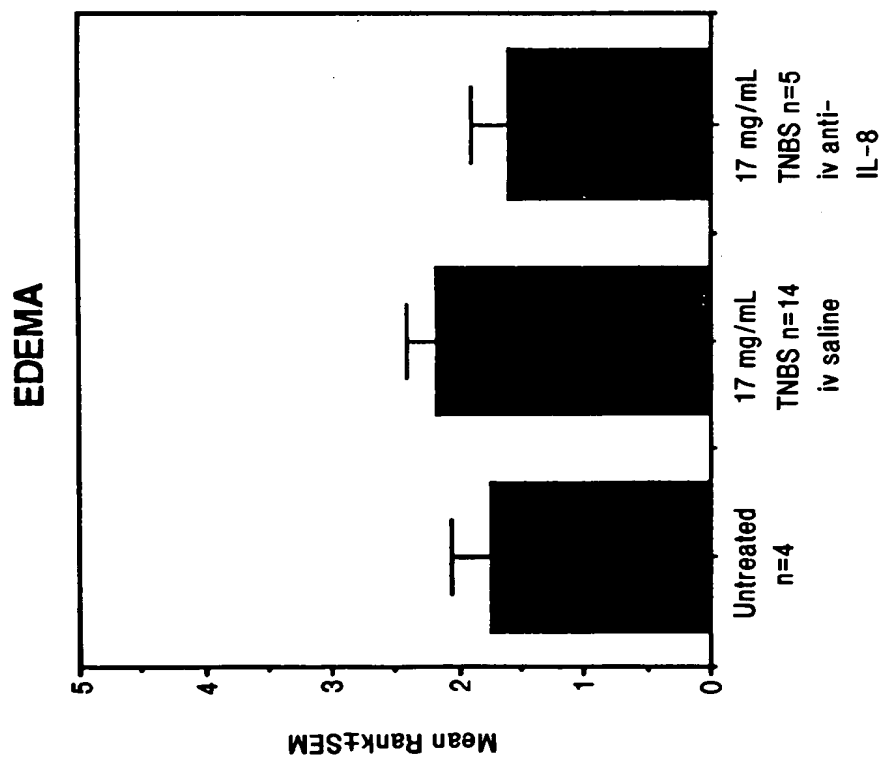


FIG. 11E



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
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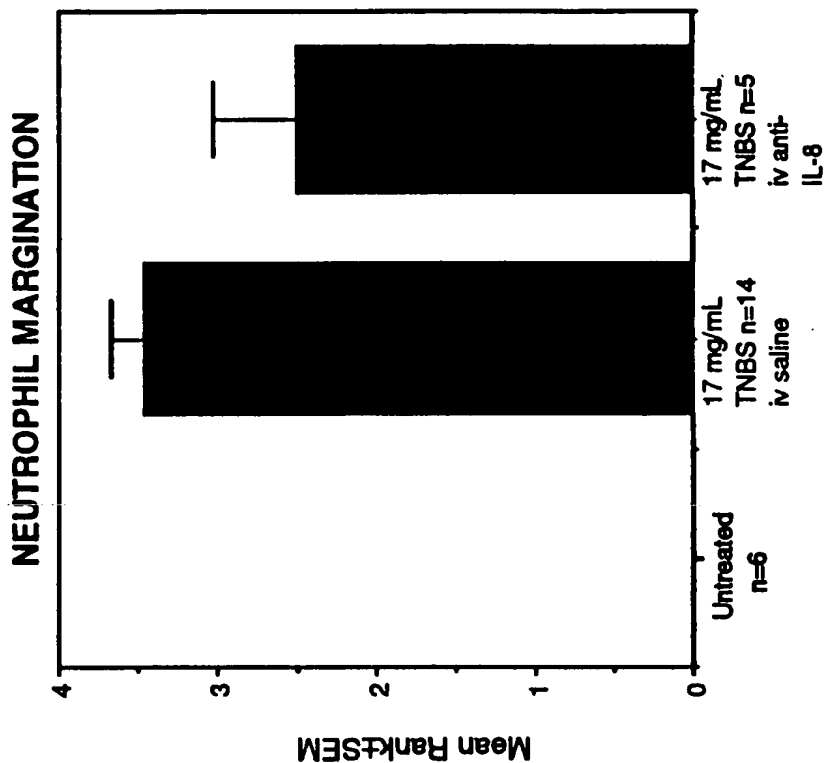


FIG. 11H

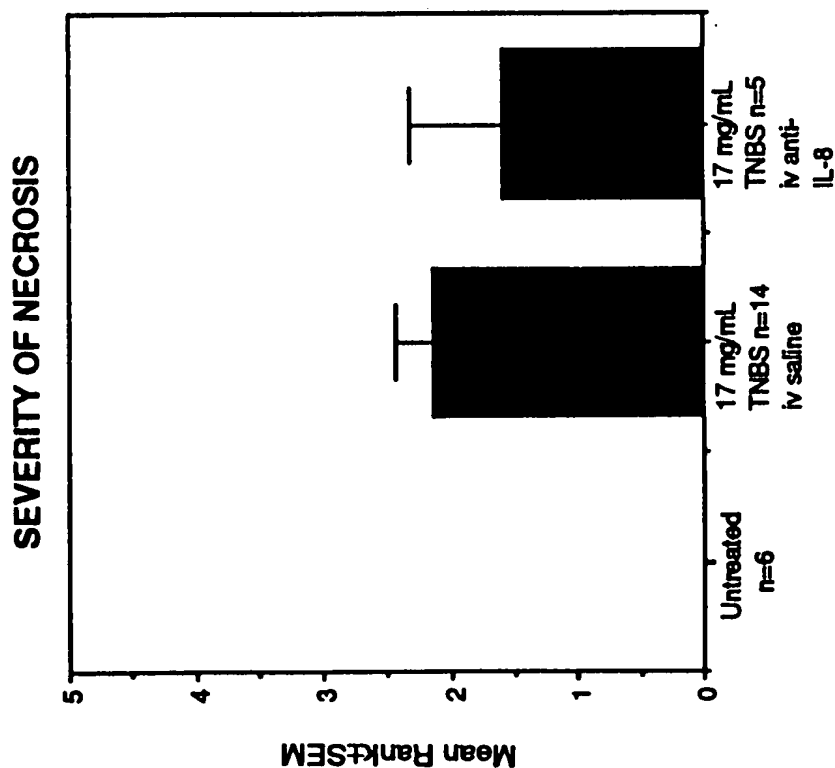


FIG. 11G



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
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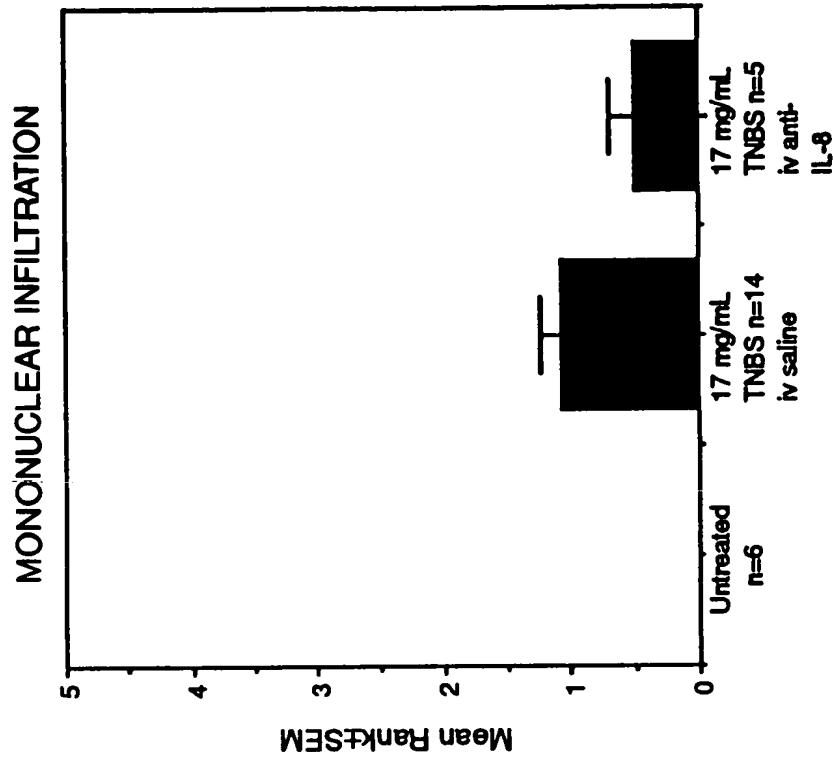


FIG. 11J

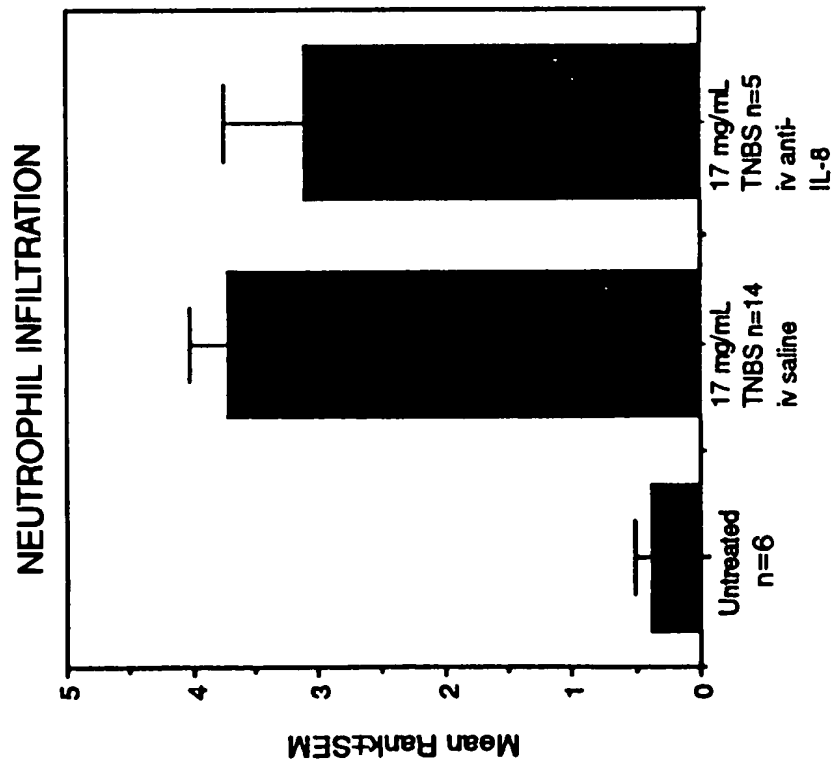


FIG. 11I

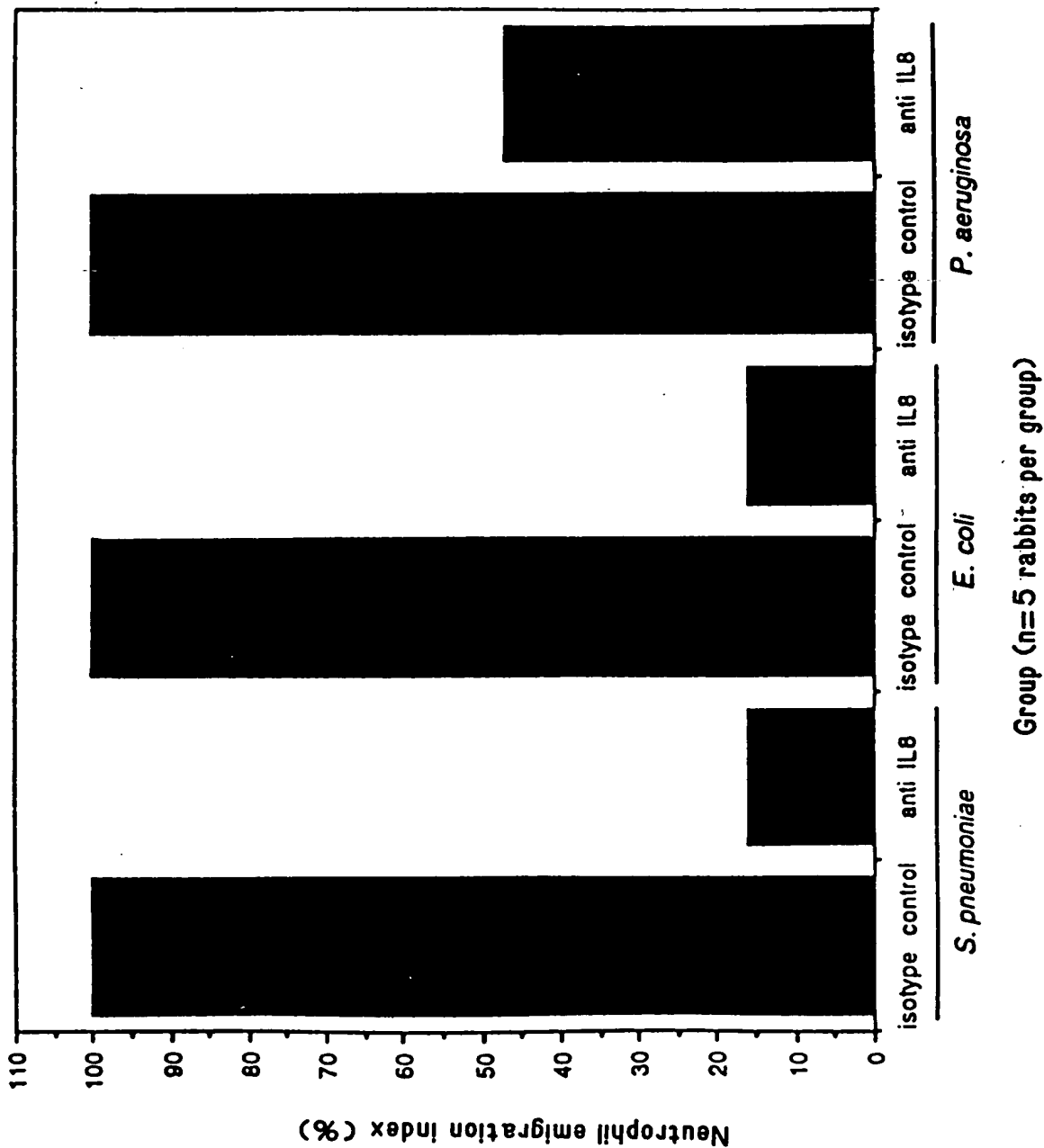


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
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FIG. 12





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
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Light Chain Primers:

MKLC-1, 22mer

FIG. 13

5' CAGTCCAAGTGTTCAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGCC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
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FIG. 14

Light chain forward primer

SL001A-2 35 mer

5' ACAACGCGTACGCT GACATCGTCATGACCCAGTC 3' (SEQ ID NO.7)
T T T A
(SEQ ID NO.8)
(SEQ ID NO.9)

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGGAAGATGGATACAGTTGGTGC 3' (SEQ ID NO.10)



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
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FIG. 15

Heavy chain forward primer

SL002B 39 mer

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTGGC 3' (SEQ ID NO.11)
T C (SEQ ID NO.12)
G (SEQ ID NO.13)
A (SEQ ID NO.14)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTGGC 3' (SEQ ID NO.11)
T (SEQ ID NO.15)
A (SEQ ID NO.14)
G (SEQ ID NO.13)



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1 GACATTGTCA TGACACAGTC TCAAAAATTC ATGTCCACAT CAGTAGGAGA CAGGGTCAGC
CTGTAACAGT ACTGTGTCAG AGTTTAAAG TACAGGTGTA GTCATCCTCT GTCCCAGTCG
1 D I V M T Q S Q K F M S T S V G D R V S

61 GTCACCTGCA AGGCCAGTCA GAATGTGGT ACTAATGTAG CCTGGTATCA ACAGAAACCA
CAGTGGACGT TCCGGTCAGT CTTACACCCA TGATTACATC GGACCATAGT TGTCCTTTGGT
21 V T C K A S Q N V G T N V A W Y Q Q K P

CDR #1

121 GGGCAATCTC CTAAAGCACT GATTTACTCG TCATCCTACC GGTACAGTGG AGTCCCTGAT
CCCCGTTAGAG GATTTCTGTA CTAAATGAGC AGTAGGATGG CCATGTCACC TCAGGGACTA
41 G Q S P K A L I Y S S Y R Y S G V P D

CDR #2

181 CGCTTCACAG GCAGTGGATC TGGACAGAT TTCACTCTCA CCATCAGCCA TGTGCAGTCT
CGGAAGTGTC CGTCACCTAG ACCCTGTCTA AAGTGAGAGT GGTAGTCGGT ACACGTCAGA
61 R F T G S G S G T D F T L T I S H V Q S

241 GAAGACTTGG CAGACTATT CTGTCAGCAA TATAACATCT ATCCTCTCAC GTTCGGTCCT
CTTCTGAACC GTCTGATAAA GACAGTCGTT ATATTGTAGA TAGGAGAGTG CAAGCCAGGA
81 E D L A D Y F C Q Q Y N I Y P L T F G P

CDR #3

301 GGGACCAAGC TGGAGTTGAA ACGGGCTGAT GCTGCACCAC CAACTGTATC CATCTTCCCA
CCCTGGTTCG ACCTCAACTT TGCCCGACTA CGACGTGGTG GTTGACATAG GTAGAAGGT
101 G T K L E L K R A D A A P P T V S I F P

BstBI

361 CCATTTCGAA (SEQ ID NO.16)

GGTAAGCTT

121 P F E (SEQ ID NO.17)

FIG. 16



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
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1 TTCTATTGCT ACAAACGCGT ACGCTGAGGT GCAGCTGGTG GAGTCTGGGG GAGGCTTAGT
AAGATAACGA TGTTTGCGCA TGC GACTCCA CGTCGACCAC CTCAGACCCC CTCCGAATCA
1 E V Q L V E S G G G L V

61 GCCGCCTGGA GGGTCCCTGA AACTCTCCTG TGCAGCCTCT GGATTCATAT TCAGTAGTTA
CGGCGGACCT CCCAGGGACT TTGAGAGGAC ACGTCGGAGA CCTAAGTATA AGTCATCAAT
13 P P G G S L K L S C A A S G F I F S S Y
* *

CDR #1

121 TGGCATGTCT TGGGTTCGCC AGACTCCAGG CAAGAGCCTG GAGTTGGTCTG CAACCATTA
ACCGTACAGA ACCCAAGCGG TCTGAGGTCC GTTCTCGGAC CTCAACCAGC GTTGGTAATT
33 G M S W V R Q T P G K S L E L V A T I N
* * *

181 TAATAATGGT GATAGCACCT ATTATCCAGA CAGTGTGAAG GGCCGATTCA CCATCTCCCG
ATTATTACCA CTATCGTGGA TAATAGGTCT GTCACACTTC CCGGCTAAGT GGTAGAGGGC
53 N N G D S T Y Y P D S V K G R F T I S R
* * * * *

CDR #2

241 AGACAATGCC AAGAACACCC TGTACCTGCA AATGAGCAGT CTGAAGTCTG AGGACACAGC
TCTGTTACGG TTCTTGTTGGG ACATGGACGT TTA CTGTCGTA GACTTCAGAC TCCTGTGTCTG
73 D N A K N T L Y L Q M S S L K S E D T A

301 CATGTTTTAC TGTGCAAGAG CCCTCATTAG TTCGGCTACT TGGTTTGGTT ACTGGGGCCA
GTACAAAATG ACACGTTCTC GGGAGTAATC AAGCCGATGA ACCAAACCAA TGACCCCGGT
93 M F Y C A R A L I S S A T W F G Y W G Q
* * * * *

CDR #3

361 AGGGACTCTG GTCACTGTCT CTGCAGCCAA AACAACAGCC CCATCTGTCT
TCCCTGAGAC CAGTGACAGA GACGTCGGTT TTGTTGTCTGG GGTAGACAGA
113 G T L V T V S A A K T T A P S V Y

411 ApaI
ATCCGGG (SEQ ID NO.18)
TAGGCCC

130 P (SEQ ID NO.19)

FIG. 17



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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FIG. 18

VL.front 31-MER

5' ACAAACGCGTACGCTGATATCGTCATGACAG 3' (SEQ ID NO.20)

VL.rear 31-MER

5' GCAGCATCAGCTCTTCGAAGCTCCAGCTTGG 3' (SEQ ID NO.21)

VH.front.SPE 21-MER

5' CCACTAGTACGCAAGTTCACG 3' (SEQ ID NO.22)

VH.rear 33-MER

5' GATGGGCCCTTGGTGGAGGCTGCAGAGACAGTG 3' (SEQ ID NO.23)

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1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCTG TTTTCTCTAT TGCTACAAAC
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG ATATCGTCAT GACACAGTCT CAAAAATTCA TGTCCACATC AGTAGGAGAC
CGCATGCGAC TATAGCAGTA CTGTGTCAGA GTTTTAAAGT ACAGGTGTAG TCATCCTCTG
-3 A Y A D I V M T Q S Q K F M S T S V G D

121 AGGGTCAGCG TCACCTGCAA GGCCAGTCAG AATGTGGGTA CTAATGTAGC CTGGTATCAA
TCCCAGTCGC AGTGGACGTT CCGGTCAGTC TTACACCCAT GATTACATCG GACCATAGTT
18 R V S V T C K A S Q N V G T N V A W Y Q
* * * * *

CDR #1

181 CAGAAACCAG GGCAATCTCC TAAAGCACTG ATTTACTCGT CATCCTACCG GTACAGTGGA
GTCTTTGGTC CCGTTAGAGG ATTTCTGTGAC TAAATGAGCA GTAGGATGGC CATGTCACCT
38 Q K P G Q S P K A L I Y S S S Y R Y S G
* * * * *

CDR #2

241 GTCCCTGATC GCTTCACAGG CAGTGGATCT GGGACAGATT TCACTCTCAC CATCAGCCAT
CAGGGACTAG CGAAGTGTCC GTCACCTAGA CCCTGTCTAA AGTGAGAGTG GTAGTCGGTA
58 V P D R F T G S G S G T D F T L T I S H

301 GTGCAGTCTG AAGACTTGGC AGACTATTTT TGTCAGCAAT ATAACATCTA TCCTCTCACG
CACGTCAGAC TTCTGAACCG TCTGATAAAG ACAGTCGTTA TATTGTAGAT AGGAGAGTGC
78 V Q S E D L A D Y F C Q Q Y N I Y P L T
* * * * *

CDR #3

BstBI

361 TTCGGTCCTG GGACCAAGCT GGAGCTTCGA AGAGCTGTGG CTGCACCATC TGTCTTCATC
AAGCCAGGAC CCTGGTTCGA CCTCGAAGCT TCTCGACACC GACGTGGTAG ACAGAAGTAG
98 F G P G T K L E L R R A V A A P S V F I

421 TTCCCGCCAT CTGATGAGCA GTTGAAATCT GGAAGTGGTT CTGTTGTGTG CCTGCTGAAT
AAGGGCGGTA GACTACTCGT CAACTTTAGA CCTTGACGAA GACAACACAC GGACGACTTA
118 F P P S D E Q L K S G T A S V V C L L N

481 AACTTCTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG ATAACGCCCT CCAATCGGGT
TTGAAGATAG GGTCTCTCCG GTTTCATGTC ACCTTCCACC TATTGCGGGA GGTTAGCCCA
138 N F Y P R E A K V Q W K V D N A L Q S G

541 AACTCCCAGG AGAGTGTACAG AGAGCAGGAC AGCAAGGACA GCACCTACAG CCTCAGCAGC
TTGAGGGTCC TCTCACAGTG TCTCGTCCTG TCGTTCCTGT CGTGGATGTC GGAGTCGTCG
158 N S Q E S V T E Q D S K D S T Y S L S S

601 ACCCTGACGC TGAGCAAAGC AGACTACGAG AAACACAAAG TCTACGCCTG CGAAGTCACC
TGGGACTGCG ACTCGTTTCG TCTGATGCTC TTTGTGTTTC AGATGCGGAC GCTTCAGTGG
178 T L T L S K A D Y E K H K V Y A C E V T

661 CATCAGGGCC TGAGCTCGCC CGTCACAAAG AGCTTCAACA GGGGAGAGTG
GTAGTCCCGG ACTCGAGCGG GCAGTGTTTC TCGAAGTTGT CCCCTCTCAC
198 H Q G L S S P V T K S F N R G E C (SEQ ID NO.25)

711 TTAA (SEQ ID NO.24)
AATT
216 O

FIG. 19



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
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1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCTG TTTTTTCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGGTGCAGCT GGTGGAGTCT GGGGGAGGCT TAGTGCCGCC TGGAGGGTCC
CGCATGCGAC TCCACGTCGA CCACCTCAGA CCCCTCCGA ATCACGGCGG ACCTCCCAGG
-3 A Y A E V Q L V E S G G G L V P P G G S

121 CTGAAACTCT CCTGTGCAGC CTCTGGATTC ATATTCAGTA GTTATGGCAT GTCTTGGGTT
GACTTTGAGA GGACACGTCG GAGACCTAAG TATAAGTCAT CAATACCGTA CAGAACCCAA
18 L K L S C A A S G F I F S S Y G M S W V
* * * *

CDR #1

181 CGCCGAGACTC CAGGCAAGAG CCTGGAGTTG GTCGCAACCA TTAATAATAA TGGTGATAGC
GCGGTCTGAG GTCCGTTTETC GGACCTCAAC CAGCGTTGGT AATTATTATT ACCACTATCG
38 R Q T P G K S L E L V A T I N N N G D S
* * * * *

241 ACCTATTATC CAGACAGTGT GAAGGGCCGA TTCACCATCT CCCGAGACAA TGCCAAGAAC
TGGATAATAG GTCTGTCACA CTTCCCGGCT AAGTGGTAGA GGGCTCTGTT ACGGTTCTTG
58 T Y Y P D S V K G R F T I S R D N A K N
* * * * *

CDR #2

301 ACCCTGTACC TGCAAATGAG CAGTCTGAAG TCTGAGGACA CAGCCATGTT TTACTGTGCA
TGGGACATGG ACGTTTACTC GTCAGACTTC AGACTCCTGT GTCGGTACAA AATGACACGT
78 T L Y L Q M S S L K S E D T A M F Y C A

361 AGAGCCCTCA TTAGTTCGGC TACTTGGTTT GGTTACTGGG GCCAAGGGAC TCTGGTCACT
TCTCGGGAGT AATCAAGCCG ATGAACCAAA CCAATGACCC CGGTTCCCTG AGACCAGTGA
98 R A L I S S A T W F G Y W G Q G T L V T
* * * * *

CDR #3

ApaI

421 GTCTCTGCAG CCTCCACCAA GGGCCCATCG GTCTTCCCCC TGGCACCCCTC CTCCAAGAGC
CAGAGACGTC GGAGGTGGTT CCCGGGTAGC CAGAAGGGGG ACCGTGGGAG GAGGTTCTCG
118 V S A A S T K G P S V F P L A P S S K S

481 ACCTCTGGGG GCACAGCGGC CCTGGGCTGC CTGGTCAAGG ACTACTTCCC CGAACCGGTG
TGGAGACCCC CGTGTCGCCG GGACCCGACG GACCAGTTCC TGATGAAGGG GCTTGGCCAC
138 T S G G T A A L G C L V K D Y F P E P V

541 ACGGTGTCGT GGAATCAGG CGCCCTGACC AGCGGCGTGC ACACCTTCCC GGCTGTCTTA
TGCCACAGCA CCTTGAGTCC GCGGGACTGG TCGCCGCACG TGTGGAAGGG CCGACAGGAT
158 T V S W N S G A L T S G V H T F P A V L

601 CAGTCCTCAG GACTCTACTC CCTCAGCAGC GTGGTGACCG TGCCCTCCAG CAGCTTGGGC
GTCAGGAGTC CTGAGATGAG GGAGTCGTCG CACCACTGGC ACGGGAGGTC GTCGAACCCG
178 Q S S G L Y S L S S V V T V P S S S L G

FIG. 20A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA
TGGGTCCTGGA TGTAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT
198 T Q T Y I C N V N H K P S N T K V D K K
721 GTTGAGCCCA AATCTTGTA CAAACTCAC ACATGA (SEQ ID NO.26)
CAACTCGGT TTAGAACACT GTTTGAGTG TGTACT
218 V E P K S C D K T H T O (SEQ ID NO.27)

FIG. 20B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAACTGTTTCAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)

FIG. 21



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
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Light chain forward primer

6G4.light.Nsi 36-MER

5'	CCAATGCATACGCT	GAC	ATC	GTG	ATG	ACC	CAG	ACC	CC	3'	(SEQ ID NO.28)
		T	T			T			T		(SEQ ID NO.29)
						A			A		(SEQ ID NO.30)

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3' (SEQ ID NO.31)

FIG. 22



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
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Heavy chain forward primer

6G4.heavy.Mlu 32-MER

5' CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG 3' (SEQ ID NO.32)
T C (SEQ ID NO.33)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCGG ATAGACCGATGGGCTGTGTTTGGC 3' (SEQ ID NO.11)
T A G (SEQ ID NO.15)
(SEQ ID NO.14)
(SEQ ID NO.13)

FIG. 23



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

70 G ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT
C TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
1 D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCAG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT
GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
18 Q A S I S C R S S O S L V H G I G N T Y
* * * * *
CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
AATGTAACCA TGGACGTCTT CCGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG
38 L H W Y L Q K P G Q S P K L L I Y K V S
* * * * *
CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTTACA
TTGGCTAAAA GACCCCAAGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
58 N R F S G V P D R F S G S G S G T D F T
* * * * *

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
78 L R I S R V E A E D L G L Y F C S Q S T
* * * * *
CDR #3

361 CATGTTCCGC TCACGTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGATGCTGCA
GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCG ACTACGACGT
98 H V P L T F G A G T K L E L K R A D A A
* * * * *

MunI

421 CCAACTGTAT CCATCTTCCC ACCATCCAGT GAGCAATTGA (SEQ ID NO.34)
GGTTGACATA GGTAGAAGGG TGGTAGGTCA CTCGTTAACT

118 P T V S I F P P S S E Q L K (SEQ ID NO.35)

FIG. 24



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

70 G AGATTTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
C TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
1 E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTTCAGTA GCCACTACAT GCACTGGGTG
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
18 V K I S C K A S G Y S F S S H Y M H W V
* * * * *

CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
TTCGTCTCGG TACCTTTCTC GGAAGTCACC TAACCGATGT AACTAGGAAG GTTACCACTT
38 K Q S H G K S L E W I G Y I D P S N G E
* * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAGT GACATCTGTG TAGAAGGTCG
58 T T Y N Q K F K G K A T L T V D T S S S
* * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
TCTCCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC
98 R G D Y R Y N G D W F F D V W G A G T T
* * * * *

CDR #3

BstEII

ApaI

421 GTCACCGTCT CCTCCGCCAA AACCGACAGC CCCATCGGTC TATCCGGGCC
CAGTGGCAGA GGAGGCGGAT TTGGCTGTCTG GGGTAGCCAG ATAGGCCCGG
118 V T V S S A K T D S P I G L S G P

471 CATC (SEQ ID NO.36)

GTAG

135 I (SEQ ID NO.37)

FIG. 25



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3' (SEQ ID NO.39)

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3' (SEQ ID NO.40)

SYN.Apa 22 MER

5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

FIG. 26

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301 2 1 2002
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1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCTG TTTTCTCTAT TGCTACAAAT
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTA
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT
CGTATGCGAC TATAGCACTA CTGTGTCCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
-3 A Y A D I V M T O T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCAG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT
GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
18 Q A S I S C R S S Q S L V H G I G N T Y
* * * * *

CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
AATGTAACCA TGGACGTCCT CGGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG
38 L H W Y L Q K P G Q S P K L L I Y K V S
* * * * *

CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTT AGTGGCAGTG GATCAGGGAC AGATTTTACA
TTGGCTAAAA GACCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
58 N R F S G V P D R F S G S G S G T D F T
* * * *

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
78 L R I S R V E A E D L G L Y F C S Q S T
* * * *

CDR #3

361 CATGTTCCGC TCACGTTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGTGTGCTGCA
GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTTCGACCTCG ACTTTGCCCG ACAACGACGT
98 H V P L T F G A G T K L E L K R A V A A
* * * * *

421 CCAACTGTAT TCATCTTCCC ACCATCCAGT GAGCAATTGA AATCTGGAAC TGCCTCTGTT
GGTTGACATA AGTAGAAGGG TGGTAGGTCA CTCGTTAACT TTAGACCTTG ACGGAGACAA
118 P T V F I F P P S S E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCCTCTCA CAGTGTCTCG TCCTGTCTGT CCTGTCTGTG

158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCTCTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

FIG. 27A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCGGACTCG AGCGGCAGT GTTCTCGAA GTTGTCCCT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAA (SEQ ID NO.41)

CTCACAATT

218 E C O (SEQ ID NO.42)

FIG. 27B

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A



1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGATTTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
CGCATGCGAC TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
-3 A Y A E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTTCAGTA GCCACTACAT GCACTGGGTG
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
18 V K I S C K A S G Y S F S S H Y M H W V
* * * * *

CDR #1

181 AAGCAGAGCC ATGGAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
TTCGTCTCGG TACCTTTCCTC GGAAGTCACC TAACCGATGT AACTAGGAAG GTTACCACTT
38 K Q S H G K S L E W I G Y I D P S N G E
* * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAGT GACATCTGTG TAGAAGGTCTG
58 T T Y N Q K F K G K A T L T V D T S S S
* * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
TCTCCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC
98 R G D Y R Y N G D W F F D V W G A G T T
* * * * *

CDR #3

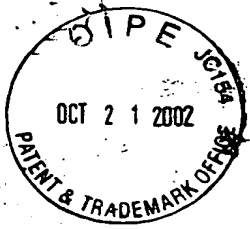
421 GTCACCGTCT CCTCCGCCTC CACCAAGGGC CCATCGGTCT TCCCCCTGGC ACCCTCCTCC
CAGTGGCAGA GGAGGCGGAG GTGGTTCCCG GGTAGCCAGA AGGGGGACCG TGGGAGGAGG
118 V T V S S A S T K G P S V F P L A P S S

481 AAGAGCACCT CTGGGGGCAC AGCGGCCCTG GGCTGCCTGG TCAAGGACTA CTTCCCCGAA
TTCTCGTGGA GACCCCGTG TCGCCGGGAC CCGACGGACC AGTTCCTGAT GAAGGGGCTT
138 K S T S G G T A A L G C L V K D Y F P E

541 CCGGTGACGG TGTCGTGGAA CTCAGGCGCC CTGACCAGCG GCGTGCACAC CTTCCCGGCT
GGCCACTGCC ACAGCACCTT GAGTCCGCGG GACTGGTTCG CGCACGTGTG GAAGGGCCGA
158 P V T V S W N S G A L T S G V H T F P A

601 GTCCTACAGT CCTCAGGACT CTACTCCCTC AGCAGCGTGG TGACCGTGCC CTCCAGCAGC
CAGGATGTCA GGAGTCCTGA GATGAGGGAG TCGTCGCACC ACTGGCACGG GAGGTCGTGC
178 V L Q S S G L Y S L S S V V T V P S S S

FIG. 28A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

661 TTGGGCACCC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC
AACCCGTGGG TCTGGATGTA GACGTTGCAC TTAGTGTTTCG GGTCTGTTGTG GTTCCACCTG
198 L G T Q T Y I C N V N H K P S N T K V D
721 AAGAAAGTTG AGCCCAAATC TTGTGACAAA ACTCACACAT GA (SEQ ID NO.43)
TTCTTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CT
218 K K V E P K S C D K T H T O (SEQ ID NO.44)

FIG. 28B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

Variable Light Chain Domain

```

10      20      abcde 30      40
6G425  DIVMTQTPLSLPVSLGDQASISCRSSQSLVHGIGNTYLHWYLQKPGQSPKLLIY
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
F(ab)-1 DIQMTQSPSSLSASVGDRTVITCRSSQSLVHGIGNTYLHWYQKPGKAPKLLIY
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
humkI   DIQMTQSPSSLSASVGDRTVITCRASKTI-----SKYLAWYQKPGKAPKLLIY
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
      =====
      ++++++++
      L1

50      60      70      80      90      100
6G425  YKVSNRFGVDPDRFSDSGSGTDFTLRISRVEAEDLGLYFCSQSTHVPLTFGAGTKLELKR (SEQ ID NO.45)
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
F(ab)-1 YKVSNRFGVPSRFSGSGSGTDFTLTISLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR (SEQ ID NO.46)
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
humkI   YSGSTLESVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHNEYPLTFGQGTKVEIKR (SEQ ID NO.47)
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
      =====
      ++++++++
      L2                                     ++++++++
      L3
```

Variable Heavy Chain Domain

```

10      20      30      40
6G425  EIQLQQSGPELMKPGASVKISCKASGYFSSHYMHVWVQSHGKSLEWI
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
F(ab)-1 EVQLVESGGGLVQPGGSLRLSCAASGYFSSHYMHVWRQAPGKGLEWV
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
humIII  EVQLVESGGGLVQPGGSLRLSCAASGFSFTGHWMNWRQAPGKGLEWV
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
      =====
      ++++++
      H1

50  a      70      80  abc      90      100      110
6G425  GYIDPSNGETTYNQKFKGKATLTVDTSSTANVHLSSLTSDDSAVYFCAARGDYRYNGDWFFDVWGAGT (SEQ ID NO.48)
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
F(ab)-1 GYIDPSNGETTYNQKFKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAARGDYRYNGDWFFDVWGQGT (SEQ ID NO.49)
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
humIII  GMIHPSDSETRYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAARGIIFY-GTTYFDYWGQGT (SEQ ID NO.50)
      #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #  #
      =====
      ++++++++
      H2                                     ++++++++
      H3
```

FIG. 29



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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Appl. No.: 09/234,182

Atty Docket: GENENT.093A

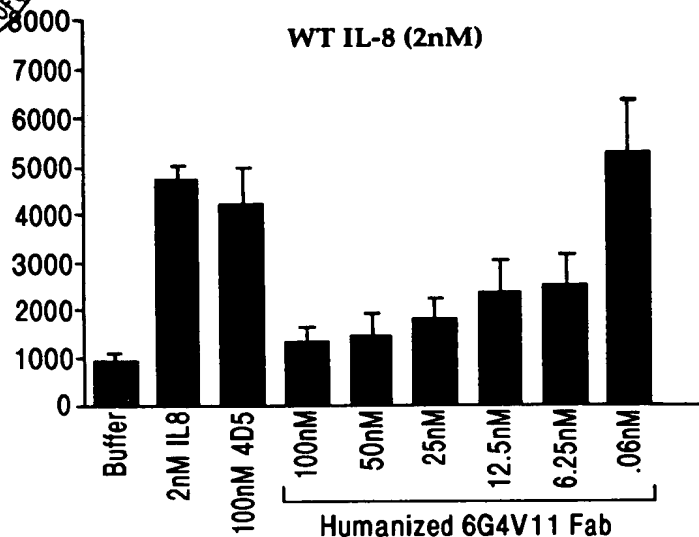


FIG. 30A

IC₅₀~12nM

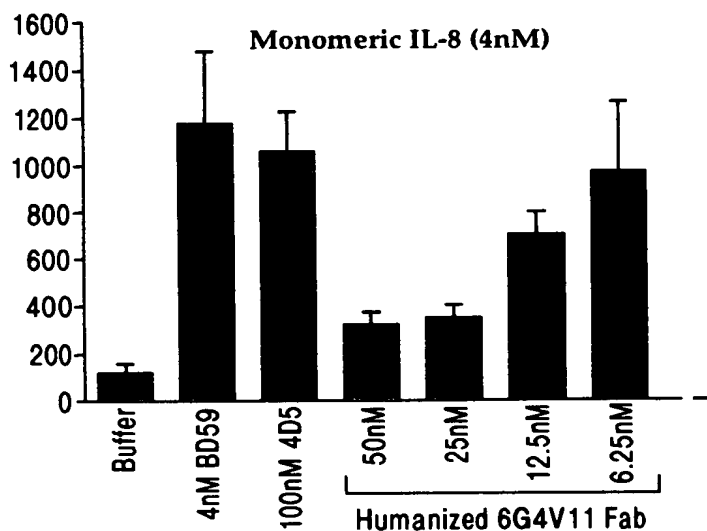


FIG. 30B

IC₅₀~15nM

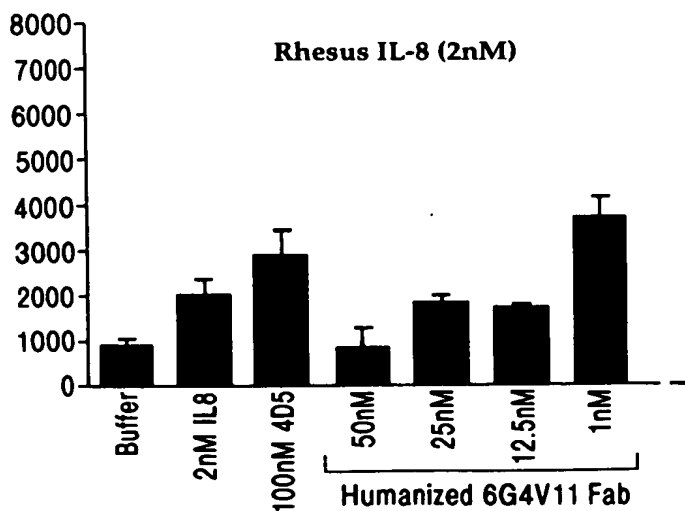


FIG. 30C

IC₅₀~22nM



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTTITCRSSQSLVHGIGNTY
LHWYQQKPKAPKLLIYKVSNRFSGVPSRFSGSGTDFTLTISLQPEDFATYYCSQST
HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKLEWVGVIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.52)

Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGSGSGDFDYKMANANKAMTENADENALQSDAKGLDSVATDYGAIDGFIGDVS
GLANGGATGDFAGSSNSQMAQVGDGDN SPLMNNFRQYLPQLPQSVECRPFVFSAGKPY
EFSIDCDKINLFRGVFAFLLYVATFMVVFSTFANILRNKES (SEQ ID NO.53)

FIG. 31A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

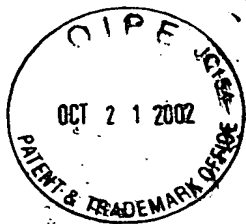
Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N
61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D
121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TAACACGTAT
TCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S Q S L V H G I G N T Y
181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S
241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T
301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T
361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A
421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V
481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N
541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCATTGAG GGTCTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCTGTTG
158 A L Q S G N S Q E S V T E Q D S K D S T
601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y
661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGACTCG AGCGGGCAGT GTTTCTCGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G
721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.51)

(SEQ ID NO.54)

FIG. 31B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTITCRSSQSLVHGIGNTY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGGTDFTLTISSLQPEDFATYYCSQST
HVPLTFGGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

MKKNIAFLLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYFSSHYMH
WVKQAPGKGLEWVGYYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.55)

FIG. 31C

FIG. 32

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A





10/21/02

ANTIBODY FRAGMENT-OLIGOMER CONJUGATES AND FORMULATIONS

ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A



FIG. 32



10/21/02

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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FIG. 32





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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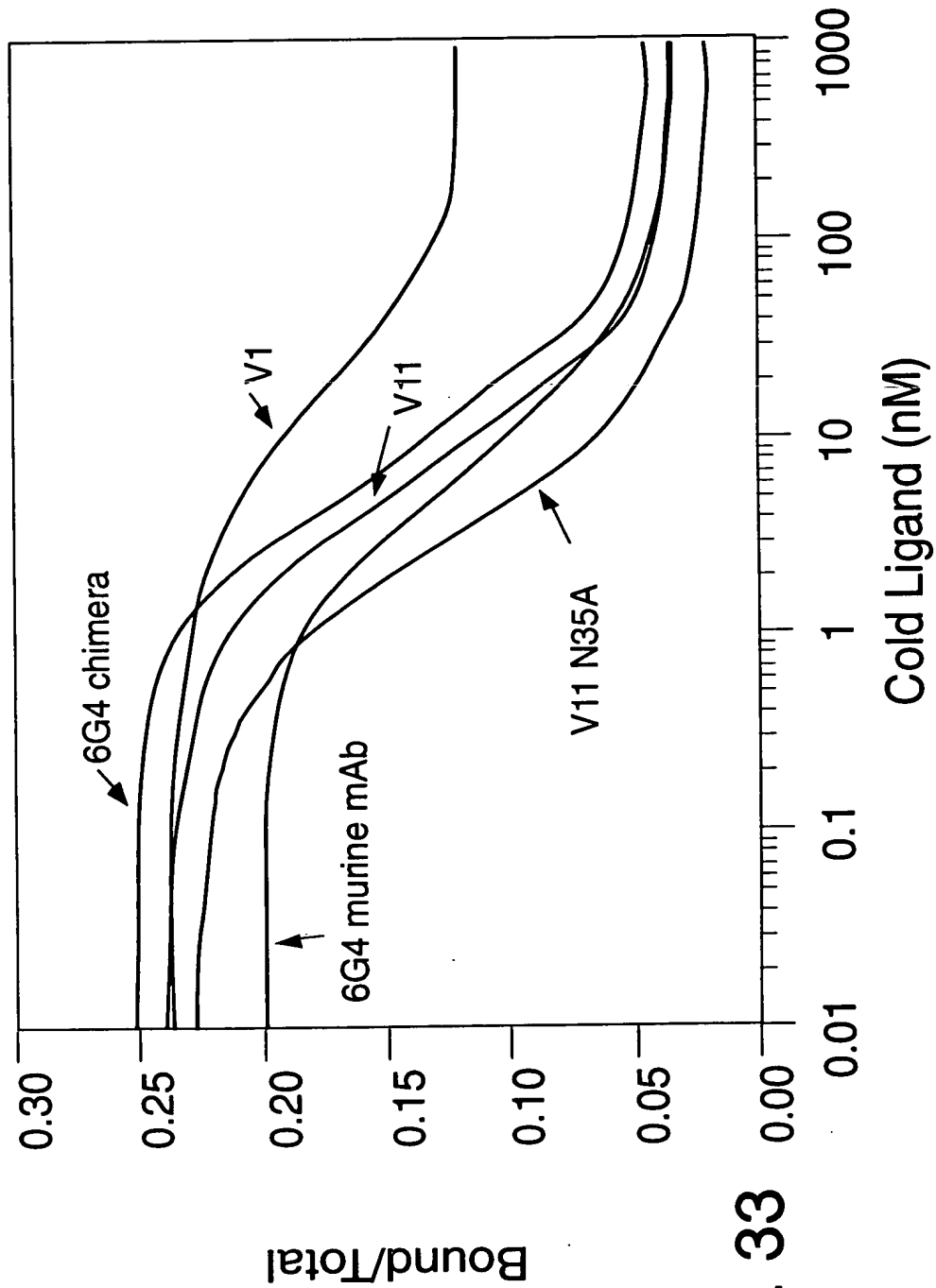
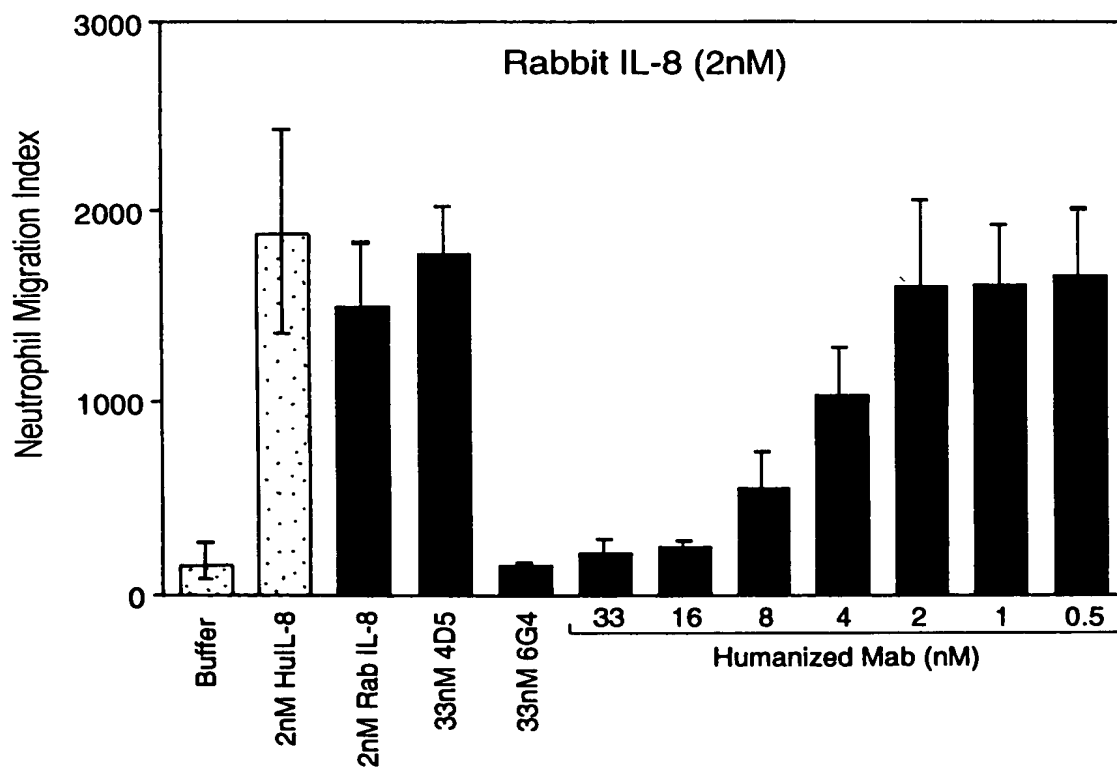
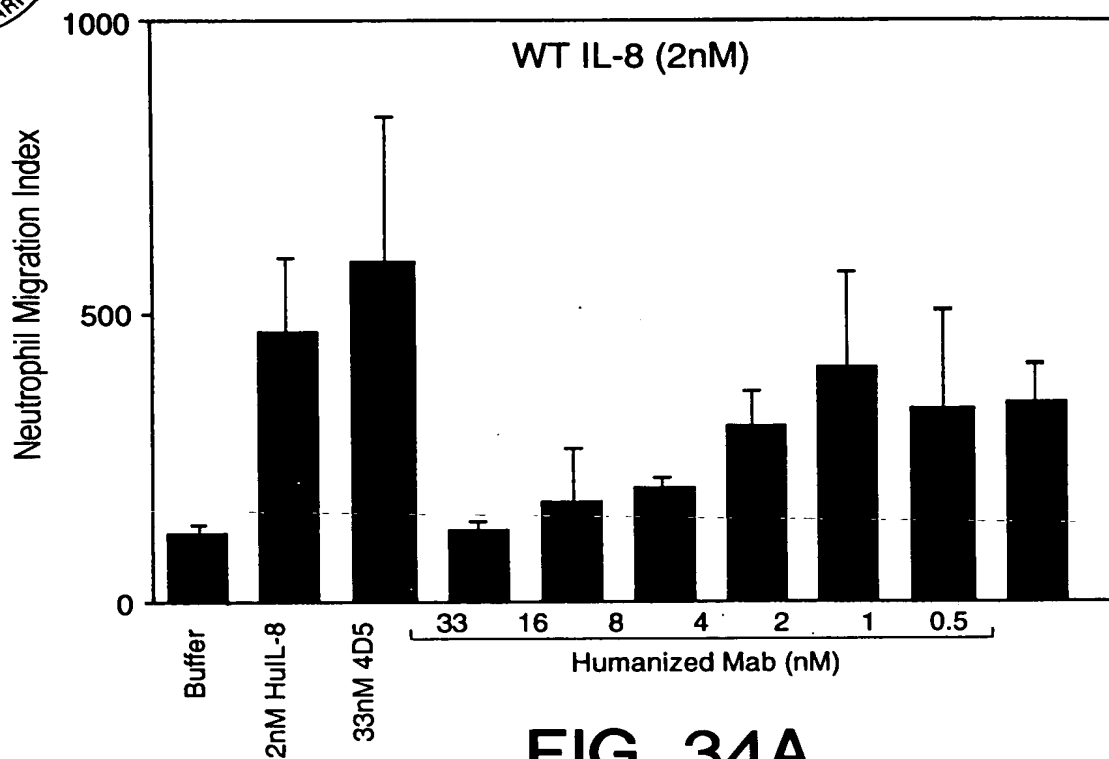


FIG. 33



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES
Hsei et al.

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ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

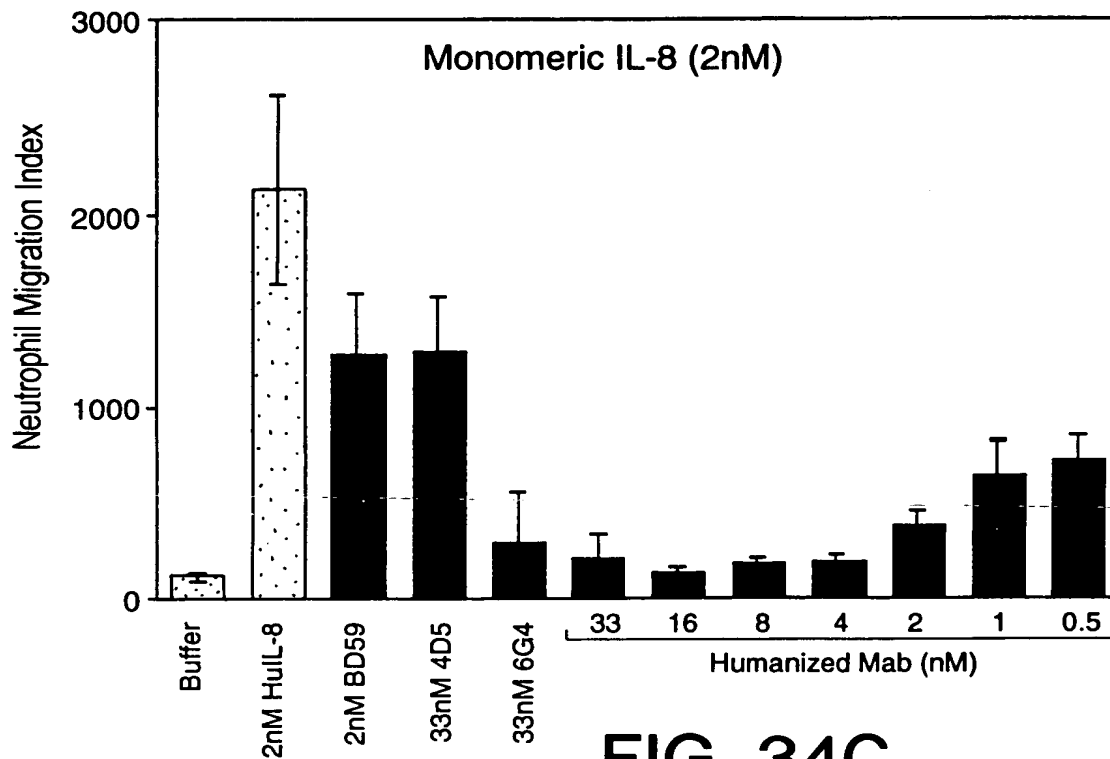


FIG. 34C

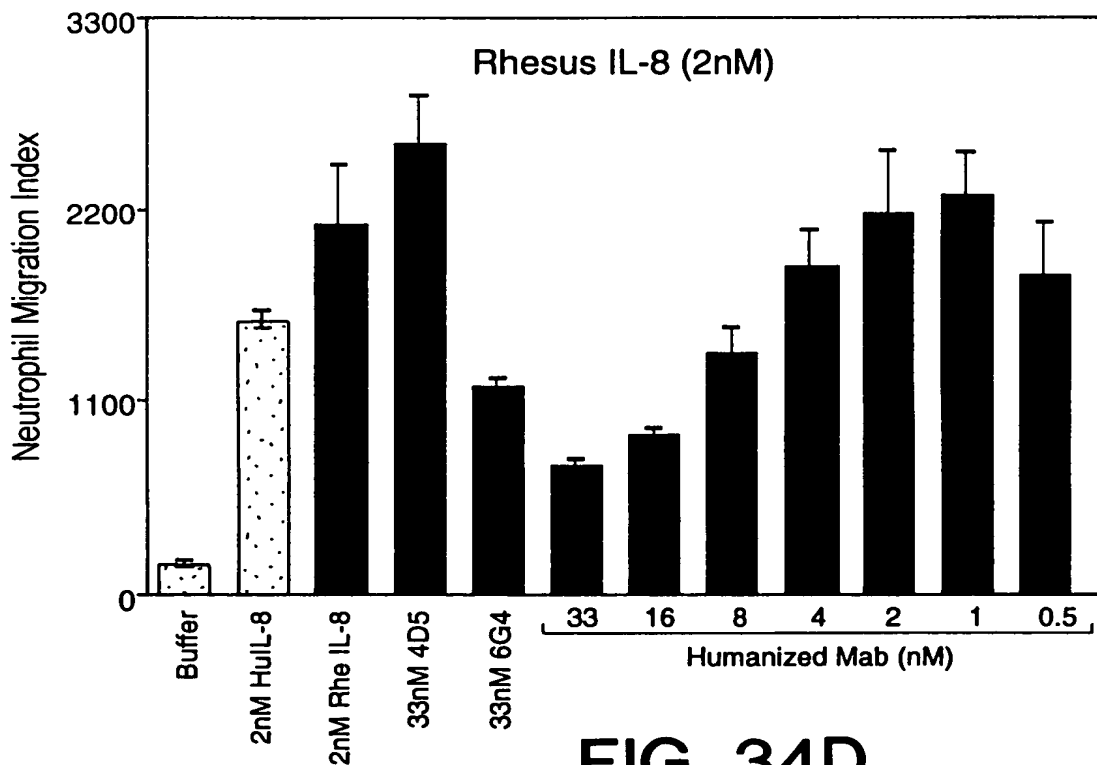


FIG. 34D



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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Atty Docket: GENENT.093A

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGATY
LHWYQQKPGKAPKLLIYKVSNRFGVPSRFGSGGTDFTLTISSLQPEDFATYYCSQST
HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.56)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLEWVGVIDPSNGETTYNQFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVY
CARGDYRYNGDWFDFVWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHPKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.52)

Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPELLGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGER (SEQ ID NO.57)

FIG. 35



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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1 ATGAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N
61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D
121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S Q S L V H G I G A T Y
181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S
241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T
301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTT ACAGAGTACT
GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T
361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A
421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V
481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N
541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCGTGG
158 A L Q S G N S Q E S V T E Q D S K D S T
601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y
661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTCTCTGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G
(SEQ ID NO.58)
721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGCACCAG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.56)

FIG. 36



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
TTTTCCCATA GATCTCCAAC TCCACTAAAA TACTTTTTTCT TATAGCGTAA AGAAGAACGT
-1 M K K N I A F L L A

841 TCTATGTTCTG TTTTTTCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT
AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
-11 S M F V F S I A T N A Y A E V Q L V Q S

901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACTATAT GCACTGGGTC CGTCAGGCC CCGGTAAGGG CCTGGAATGG
AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCATTCCC GGACCTTACC
28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
CAACTATAT AACTAGGAAG GTTACCACCTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTA CTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCTAA TAGCGATGTT ACCACTGACC
88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
AAGAAGCTGC AGACCCCAGT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCCG
108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCCGTG TCGCCGGGAC
128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
CCGACGGACC AGTTCCTGAT GAAGGGGCTT GGCCACTGCC ACAGACCTT GAGTCCGCGG
148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCTCGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
GACTGGTCGC CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCTTGA GATGAGGGAG
168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
TCGTGCGACC ACTGGCACGG GAGGTCGTCTG AACCCGTGGG TCTGGATGTA GACGTTGCAC
188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTGCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
TtagtGTTCTG GGTCGTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCCCGCCGTG CCCAGCACCA GAACTGCTGG GCGGCCGCAT GAAACAGCTA
TGAGTGTGTA CGGGCGGCAC GGGTCGTGGT CTTGACGACC CGCCGGCGTA CTTTGTCTGAT
228 T H T C P P C P A P E L L G G R M K Q L

FIG. 37A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA
CTCCTGTTCC AGCTTCTCGA TGAGAGGTTC TTGATGGTGG ATCTCTTACT TCACCGTTCT
248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA (SEQ ID NO.59)
GAGTTTTTCG AACAGCCCCT CGCGATT
268 L K K L V G E R O (SEQ ID NO.60)

FIG. 37B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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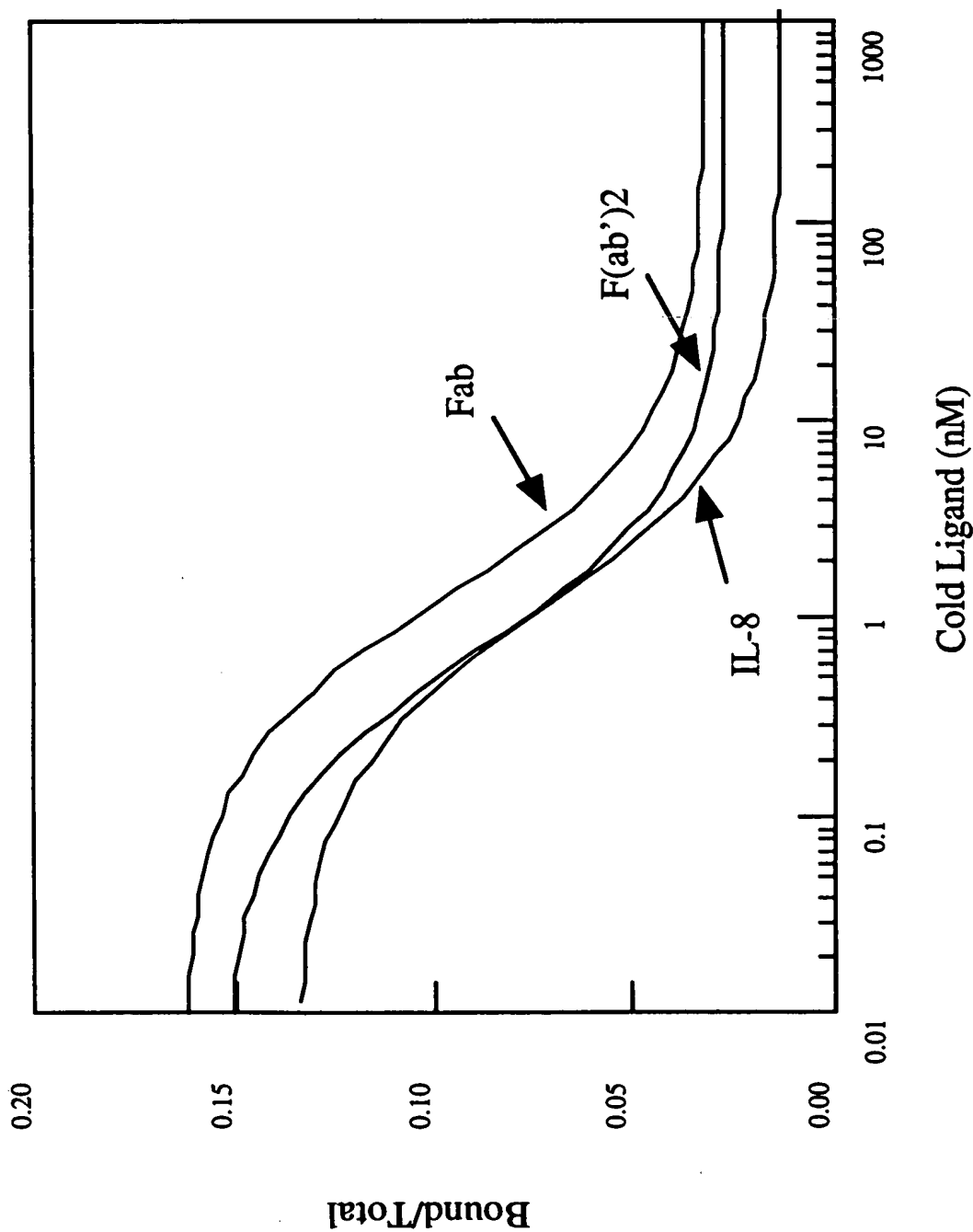


FIG. 38

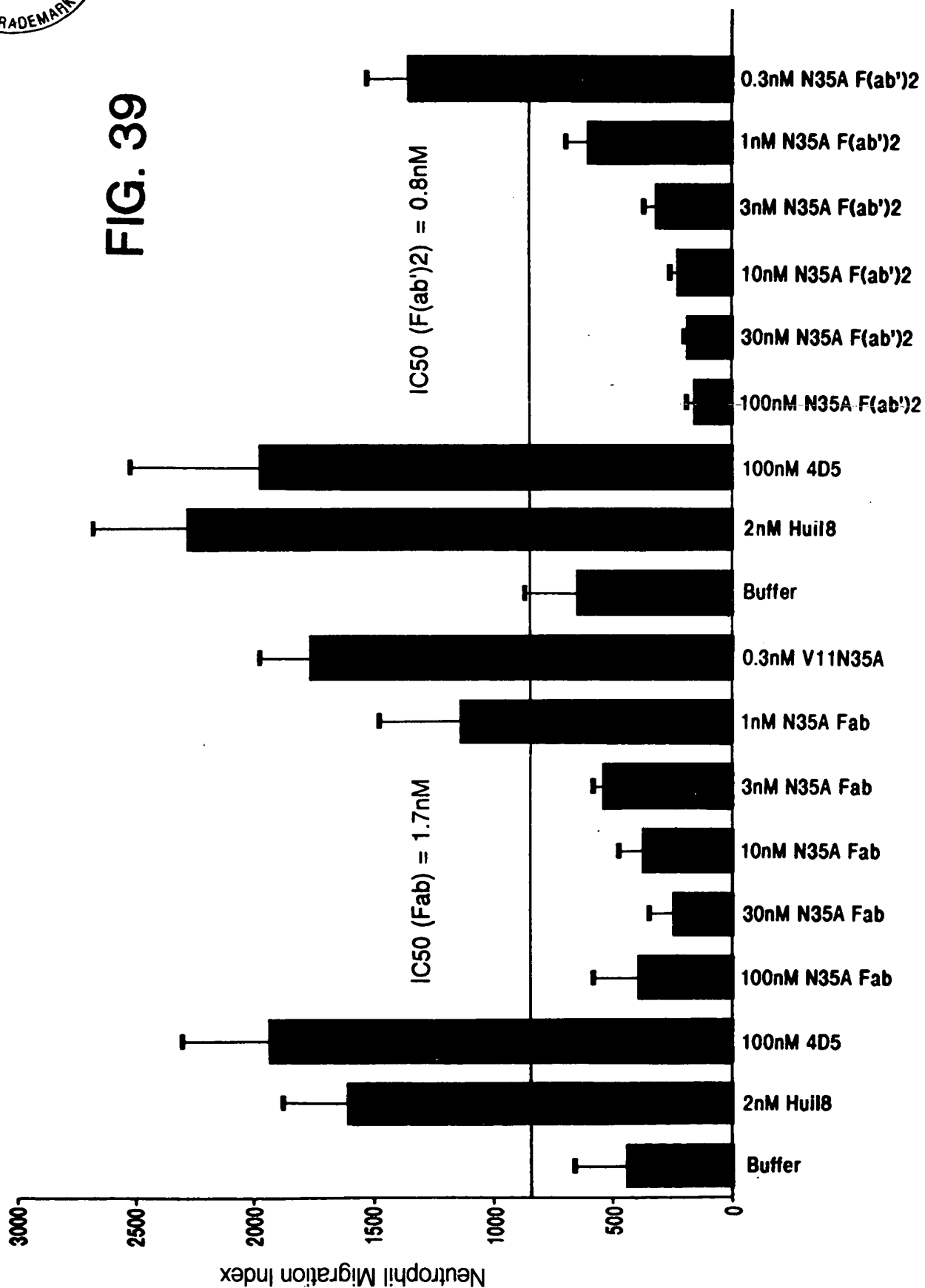


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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FIG. 39



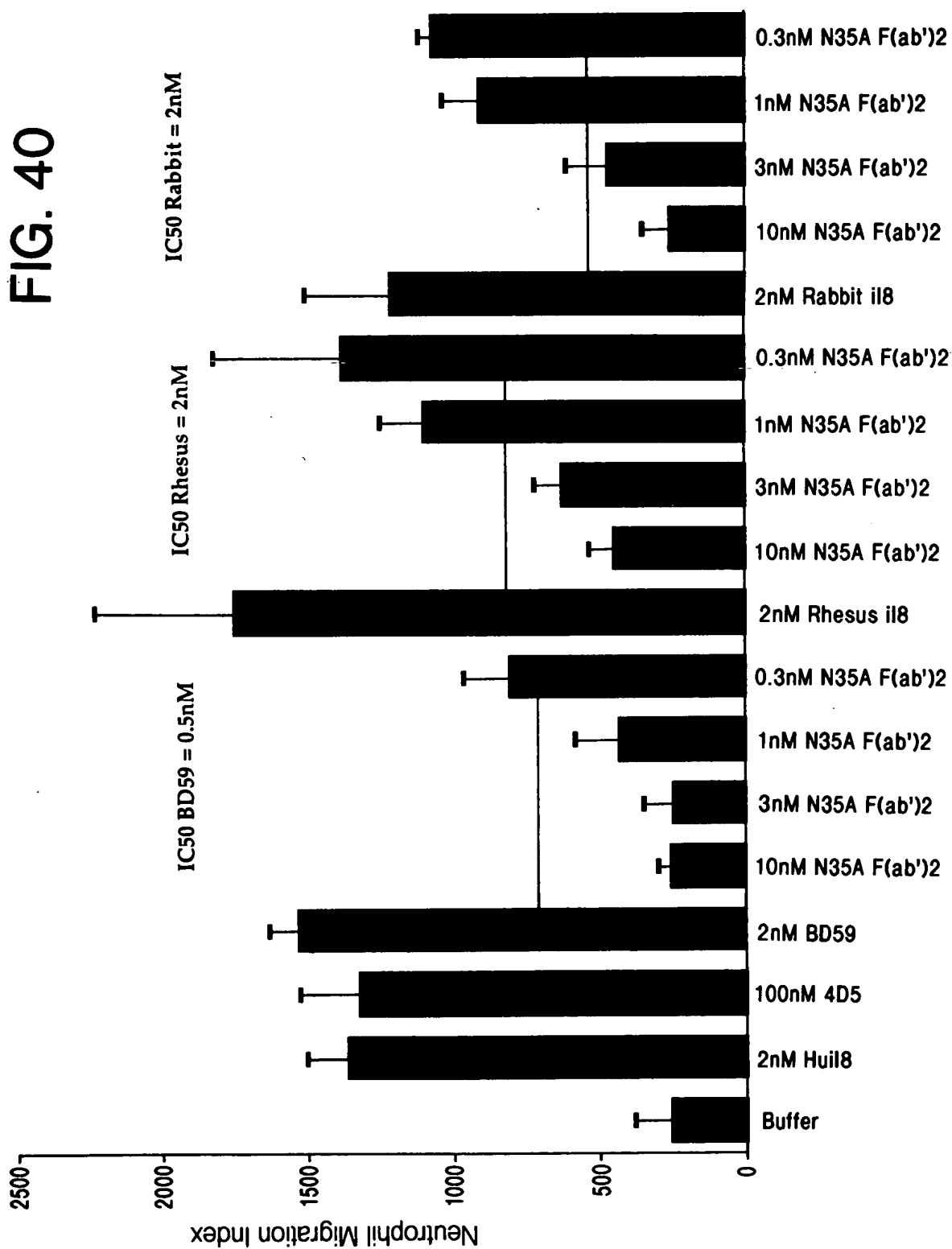


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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FIG. 40



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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ecoRI pflMI pleI
apoI bslI mboII taqI
1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATTAT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT mboII hinfI
CTTAAGTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTAC AGTAACGACT CAACAATAA TTGGAACGGG TTTTCTCTCT TCTCAGCTTA
bspMI sau3AI
hinPI mboI/ndeII[dam-]
hhaI/cfoI dpuI[dam+]
mstI mboII[dam-]
aviII/fspI hinfI acI
101 GAACGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACGG GTTGATTGAT CAGGTACAGG bclI[dam-] mnlI
CTTGACACAC CGTCCATCT TCGAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTAC TGGTTCTGCG CAACCTAACTA GTCCATCTCC
thai
fnuDII/mvni
fnu4HI
bsoFI
bbvI maeII
fnu4HI bstUI snaBI
bsoFI bsh1236I mnlI
bbvI hinPI bsaAI foki
aluI hhaI/cfoI sfanI
201 GGGCGCTGA CGAGGTAAAG CCCGATGCCA GCATTCTCTGA CGACGATACG GAGCTGCTGC CGGATTACGT AAAGAAGTTA TTGAACCATC CTCGTCAGTA
CCCCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGAGC CGCTAATGCA TTTCTTCAAT AACCTCGTAG GAGCACTCAT
haeIII/palI
mcRI
eagI/xmaIII/ecI XI
eaeI
cfrI
bsiEI ahdI/eam1105I
maeIII bsmAI
tru9I aluI
mseI pvuII
nspBII
301 AAAGTTAAT CTTTTCACA GCTGTCTATAA AGTTGTACAG CCGAGACTT ATAGTCGCTT TGTGTTTATT TTTTAATGTA TTTGTAACCTA GAATTCGAGC
TTTTCATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAATTACAT AACATTGAT CTTAAGCTCG

FIG. 41A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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scrFI
ncII
mspi
hpaII
dsav
xmaI/pspAI
smaI
scrFI
ncII
dsav
cauII
bsaJI
avaI
sau3AI taqI
mboI/ndeII[dam-]
rsal
csp6I
nlaIV
kpnI cauII dpnII[dam-]
hgiCI
bani bsaJI alwI[dam-]
asp718 bamHI avai
acc65I alwI[dam-] mnII mnII
501 TCGGTACCCG GGATCCTCT CGAGGTGAG GTGATTTTAT GAAAAGAAT ATCGCATTC TTCTTGCATC TATGTCGTT TTTTCTATTG CTACAAACGC
AGCCATGGGC CCTAGGAGA GTCCAACTC CACTAAATA CTTTCTTCTTA TAGCGTAAAG AAGAAGCTAG ATACAGCAA AAAAGATAAC GATGTTTGGC
M K K N I A F L L A S M F V F S I A T N A
a mutation was found that inactivated the mluI site. The penultimate nucleotide was changed fr G toT ^

-23

sstI
sacI
hgiJII
hgiAI/aspHI
ecII36II
bsp1286
bsiHKAI
bsmFI bmyI
bsrI avai aluI
tthIII/aspI banII
ecoRV
501 ATACGTGAT ATCCAGATGA CCCAGTCCC GAGTCCCCTG TCCGCCTCTG TGGGGGATAG GGTCACCATC ACCTGCAGGT CAAGTCAAAG CTTAGTACAT
TATGGACTA TAGTCTACT GGGTCAGGG CTCGAGGGG AGCGGGAGAC ACCCGCTATC CCAGTGGTAG TGGAGTCCA GTTCAGTTTC GAATCATGTA
-2 Y A D I Q M T Q S P S S L S A S V G D R V T I T C R S S Q S L V H

bspMI
scfI
psti
hphI sse8387I
maeII bspMI
bstEII hphI bsgI
hphI maeII bspMI
hphI sse8387I
ddeI nlaIII
aluI rsaI
hindIII csp6I
CAAGTCAAAG CTTAGTACAT
GTTCAGTTTC GAATCATGTA

FIG. 41B



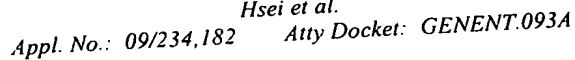
ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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scrFI
mval
ecoriI
daav
bstNI
bsaJI
maeIII apyI[dcn+]
mnII
bsII
maeIII apyI[dcn+]
201 TCTGGAAGTGT GTGCTGTGTGT GTGCTGTGTGT ATCCACAGAG GGCACAAAGTA CAGTGAAGG TGGATAACGC CCTCCAATCG GGTAACCTCCC
AGACCTTGAC GAAGACAACA CACGGACGAC TATATTGAAGA TAGGGTCTCT CCGGTTTCAT GTGACCTTCC ACCTATTGCG GGAGGTTAGC CCATTGAGGG
132 S G T A S V V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q
haeIII/pali
haeI
mnII
rsal
csp6I
fnu4HI
bsoFI
ddei
scFI
mnII
bbVI
hgaI
ddei
celII/espi
bipi/bpul102I
accI
cac8I
1001 AGGAGAGTGT CACAGAGCAG GACAGCAAGG ACAGCACCTA CAGCCTCAGC AGCACCTGA CGCTGAGCAA AGCAGACTAC GAGAAACACA AAGTCTACGC
TCCTCTCACA GTGCTGTGTC CTGTGTGTC GTGTGTGTC GTGTGTGTC GTGTGTGTC GTGTGTGTC GTGTGTGTC GTGTGTGTC GTGTGTGTC GTGTGTGTC
166 E S V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A
cac8I
aluI
sstI
sacI
hgiJII
hgiAI/aspHI
ecII36II
bsp1286
bsiHKAI
bmyI
haeIII/pali
sau96I
banII
asuI
ddei
hphI
eco0109I/draiI
maeIII
aluNI[dcn-]
maeIII
alwNI[dcn-]
GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC
1101 CTGCGAAGTC ACCCATCAGG GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC GCTGTGAGTC
GACGCTTCAG TGGGTAGTCC CGGACTCGAG CGGCGAGTGT TTCTCGAAGT TGTCCTCTCT CACAATTGCA GTAGGAGATG CGGCTGCGT AGCACCGGGA
199 C E V T H Q G L S S P V T K S F N R G E C O (SEQ ID NO.56)
maeIII
aluNI[dcn-]
hgaI
tru9I
dpnII[dam-]
mspI
aluI
dpnII[dam-]
hpaII
sfaNI
asuI
maeIII/pali
sau96I
hgaI
maeIII
bfaI
maeIII
rmaI

FIG. 41D



```
scrFI
ncil
mspi
hpail
dsav
cauli
bsli
xmai/pspai
smai
scrFI
ncil
dsav
cauli
bsli
scrFI
mval
ecorII
```


1401 CTTCTCGAGT CACTATATGC ACTGGGTCCG TCAGGCCCGG GGTAAGGCC TGAATGGGT TGGATATATT GATCCTTCCA ATGGTGAAC TAGGTATAAT
GAAGAGCTCA GTGATATACG TGACCCAGGC AGTCCGGGC CCATTCCCG ACCTTACCCA ACCTATATAA CTTAGGAAGGT TACCACCTTG ATGCATATTA
29 F S S H Y M H W V R Q A P G K G L E W V G Y I D P S N G E T T Y N

1501 CAAAAGTTCA AGGCCCGTTT CACTTTATCT CGCGACAAC CCAAAAACAC AGCATACCTG CAGATGAACA GCGTGGTGC TCAGGACACT GCCGTCTATT
GTTTTCAGT TCCCGGCAAA GTGAATAGA GCGCTGTTGA GGTTTTGTG TCGTATGGAC GTCTACTGT CCGACGCACG ACTCCTGTGA CGGCAGATAA
62 Q K F K G R F T L S R D N S K N T A Y L Q M N S L R A E D T A V Y Y

1601 ACTGTGCAAG AGGGGATTAT CGGTACAATG GTGACTGGT CTTTCGAGTC TGGGGTCAAG GAACCTGTG CACCGTCTCC TCGGCTTCCA CCAAGGCCCC
TGACACGTTT TCCCTTAATA GCGATGTTAC CACTGACCAA GAAGCTGCAG ACCCAGTTC CTTGGGACCA GTGGCAGAG AGCCGAGGT GGTTCGCGG
96 C A R G D Y R Y N G D W F F D V W G Q G T L V T V S S A S T K G P

seq right is from p6G425chim2.fab2

FIG. 41E



1701 ATCGGTCTTC CCCCTGGCAC CCTCTCCAA GAGCAGCTCT GGGGGCACAG CGGCCCTGGG CTGCTGTGTC AAGGACTACT TCCCCGAACC GGTGACGGTG
TAGCCAGAG GGGGACCGTG GGAGGAGTT CTCGTGGAGA CCCCCTGTC GCGGGACCC GACGGACCCAG TTCCTGATGA AGGGGCTTG CCACCTGCCAC
129 S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P V T V

196 S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S C D K T

1901 CCAGCAGCTT GGGCACCAG ACCCTACATCT GCAAGCTGAA TCACAAGCCC AGCAACACCA AGGTGACAA GAAAGTTGAG CCCAAATCTT GTGACAAAAC
GGTCGTGAA CCCGTGGTC TGGAGTAGA CGTGTGACTT AGTGTGCGG TCGTGTGGG TCCAGCTGT TTTCAACTC GGGTTAGAA CACTGTTTG

196 S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S C D K T

FIG. 41G



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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fnu4HI
bsoFI
haeIII/palI
mcrI
eagI/xmaIII/ecI XI
eaeI
cfrI
bsiEI
notI
fnu4HI
bsoFI
nlalIII
acII acI
cac8I
nlalIII
nspI
nspHI
acII bmyI
bspl286
2001 TCACACATGC CCGCGTGCC CAGCACCAGA ACTGCTGGC GCGCGCATGA AACAGCTAGA GGACAAGGTC GAAGAGCTAC TCTCCAAGAA CTACCACCTA
AGTGTGTACG GCGGCGACCG GTGCTGGTCT TGACGACCG CCGCGGTACT TTGTCGATCT CCTGTTCCAG CTTCTCGATG AGAGGTCTT GATGGTGGAT
229 H T C P P C P A P E L L G G R M K Q L E D K V E E L L S K N Y H L
^junction between antibody and leucine zipper

sphi
ddeI nlalIII
celII/espi
blpI/bpull02I
hinPI nspi
hhai/cfoI
haeII nspHI
eco47III cac8I
pleI aluI
hinFI hindIII
GAGAATGAAG TGGCAAGACT CAAAAGCTT GTCGGGAGC GCTAAGCATG CGACGGCCCT AGAGTCCCTA ACCTCGGT GCCGCCGCC GTTTTTTTATT
CTCTTACTC ACCGTTCTGA GTTTTTCGAA CAGCCCTCG CGATTCGTAC GCTGCCGGA TCTCAGGAT TCGAGCCAA CGCGGCCCG CAAAAAATAA
262 E N E V A R L K L V G E R O (SEQ ID NO.60)

truu9I
mseI
hpaI nlalIII
hincII/hindII
aluI
2201 GTTAACATCAT GTTTGACAGC TTATCATCGA TAAGCTTAA TCGGCTAGTT TATCAGAGTT AAATTGCTAA CGCAGTCAGG CACCGTGTAT GAAATCTAAC
CAATTGAGTA CAAACTGTG AATAGTAGCT ATTGGAATT ACGCCATCA AATAGTCA TTTAACGATT GGTTCAGTCC GTGGCACATA CTTTAGATTG

nlalIV
hgICI
bani
```

FIG. 41H

FIG. 41I

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES

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2601
2801

2701

2801

FIG. 41J

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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```

sau3AI
mboI/ndelII[dam-]
mamI[dam-]
dpmI[dam+]
dpmII[dam-]
bstYI/xhoII
alwI[dam-]
mspI
hpaII
mroI bsabI[dam-] fnu4HI
bspMII bsoFI
bspEI[dam-] bbvI
bsaWI sfaNI
accIII[dam-] foki cac8I
TTATGTTCCG GATCTGCATC GCAGGATGCT GCTGGCTACC
3801 TGTGCTTCGG TTTCCGTGTT TCGTAAAGTC TGGAAACGGC GAAGTCAGCG CCTGACCA mslI
ACCAAGCC AAAGGCACA AGCATTTCAG ACCTTTGCC CTTCACTCGC GGGACGTGGT AATACAAGC CTAGACGTAG CGTCTACGA CGACCGATGG

          aciI
          thal
          fnuDII/mvnI hinPI
          bstUI hhaI/cfoI
          bsh1236I haeII mslI
          cac8I
          hinPI
          hhaI/cfoI
          tru9I haeII
          mselI ecc47III ddel
          cac8I
          hinPI
          hhaI/cfoI
          foki
          sfaNI
          nlaIV aciI
          avall fnu4HI
          asuI bsoFI
          bsmFI foki
          aciI
          bsrI
          mnlI
          nlaII apoI bslI

          nspi
          scrFI
          nclI
          mspI
          hpaII
          bsrI
          bslI
          dsav nlaII
          maelI
          cauII
          psp1406I maelII nspHI
          4001 CAACGTTCCA GTAACGGGC ATGTTTCATCA TCAGTAACCC GTATCGTGAG CATCCTCTCT CGTTTCATCG GTATCATTTAC CCCCATGAAC AGAAATTCCC
          GTTGCAAGGT CATTGGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGAGA GCAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG

```

FIG. 41N



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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```

cac8I
sau96I
tru9I haeIII/palI
mseI asuI
acuI bslI nlaIII aciI
mseI
sfanI maeIII
mnlI
4101 CCTTACACG AGGCATCAAG TGACCAACA GGA AAAAACC GCCCTTAACA TGGCCCGTT TATCAGAAGC CAGACATTAA CGCTTCTGGA GAAACTCAAC
GGAATGTGCC TCGTAGTTC ACTGGTTTGT CTTTTTTTGG CGGGAATTGT ACCGGGGGAA ATAGTCTTCG GTCTGTAATT CGGAAGACCT CTTTGAGTTG
acuI
thai
fnuDII/mvnl
bstUI
bsh1236I
aluI hgaI foki
asp700
4201 GAGCTGGACG CGGATGAACA GGCAGACATC TGTGAATCGC TTCACGACCA CGCTGATGAG CTTTACCGCA GCTGCTCGC GCGTTCGGT GATGACGGTG
CTGACCTGC GCCTACTTGT CCGTCTGTAG ACACCTTAGC AAGTGTGCTG GCGACTACTC GAAATGCGGT CGACGGAGCG CGCAAGCCCA CTACTGCCAC
aluI hgaI foki
asp700
mseI aluI aciI bsvI bsh1236I hphI
fnu4HI hpaII
bsoFI scrFI
bbvI nciI
nlaIII dsav
nspI cauII
nspHI aluI bslI maeIII
4301 AAAACCTCTG ACACATGCAG CTCCCGGAGA CGGTCACAGC TTGTCTGTAA GCGGATGCGG GGAGCAGACA AGCCCGTCAG GCGGCTCAG CGGCTGTGG
TTTTGGAGAC TGTGTACGTC GAGGCCCTCT GCCAGTGTGC AACAGACATT GCCTACGCG CCTCGTCTGT TCGGGCAGTC CGCCACACAC
```

FIG. 410



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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4401 CGGGTGTCCG GCGCGAGCCA TGACCCAGTC ACCTAGCGAT AGCGGAGTGT ATACTGGCTT AACTATGCGG CATCAGAGCA GATTGACTG AGAGTGACCC
GCCACAGCC CCGCGTCCGT ACTGGTCCAG TGCATCGCTA TCGCTCACA TATGACCGAA TTGATACGCC GTAGTCTCGT CTAACATGAC TCTCACGTGG
fnu4HI maeII
bsoFI maeIII
bbvI maeIII
hinPI nlaIII bsrI bsaAI
hhaI/cfoI tthIII/aspI
4501 ATATGCGGTG TGAATACCG CACAGATCGG TAAGGAGAAA ATACCGCATC AGCGCTCTT CCGCTTCTC GCTCACTGAC TCGCTGCGCT CGGTGTTCCG
TATACGCCAC ACTTTATGGC GTGTCTAGCC ATTCTCTTTT TATGGCGTAG TCCGCGAGAA GCGGAAGGAG CGAGTGACTG AGCGACGCGA GCCAGCAAGC
acII acII acII sfanI
4601 GCTGCGCGA GCGGTATCAG CTCACCTAAA GCGCGTAATA CGGTATATCCA CAGAATCAGG GGATAACGCA GGAAAGAACA TGTGAGCAAA AGGCCAGCAA
CGACGCGCT CGCCATAGTC GAGTGAGTTT CGCCATTAT GCCAATAGGT GTCTTAGTCC CCTATTGCGT CTTTCTTGT AACTCGTTT TCCGTCGTT
fnu4HI bsoFI acII
bsoFI bsrBI
bbvI cac8I aluI acII
4701 AAGGCCAGGA ACCGTAAAAA GCGCGGCTTG CTGGCGTTT TCCATAGGCT CCGCCCCCTT CACGAGCATC ACAAATAATCG ACGTCAAGT CAGAGGTGGC
TTCCGTCCT TGGCATTTT CCGGCGAAC GACCGCAAC GCGGCGGGA CTGCTCGTAG TGTCTTAGC TCGAGTTCA GTCTCCACCG
scrFI thaI
mvaI fnuDII/mvni
ecorII bstUI
dsav bsh1236I
bstNI bslI
apyI[dcmt+] fnu4HI
haeIII/palI bsoFI cac8I
haeI nlaIV haeIII/palI
791

FIG. 41P



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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Atty Docket: GENENT.093A

4801 GAAACCCGAC AGGACTATTA AGATACCAGG CGTTTCCCCC TGAAGCTCC CTCGTGGCT CTCCTGTTCC GACCTGCGG CTTACCGGAT ACCTGTCCGC
CTTTGGGCTG TCCTGATATT TCATGTGCTC GAAAGGGGG ACCTTCGAGG GAGCAGCGGA GAGCAGCGGA GAGCAGCGGA GAGCAGCGGA GAGCAGCGGA GAGCAGCGGA
bslI acilI mspI fnu4HI hpaII
bsaJI aluI mnlI hhaI/cfoI
bsaJI aluI mnlI hhaI/cfoI
4901 CTTTCTCCCT TCGGGAAGCG TGGCGCTTTC TCATAGCTCA CGCTGTAGGT ATCTCAGTTC GGTGTAGGTC GTTCGGCTCCA AGCTGGGCTG TGTGCACGAA
GAAAGAGGGA AGCCCTTCCG ACCCGGAAAG AGTATCGAGT GCGACATCCA TAGAGTCAAG CCACATCCAG CAAGCGAGGT TCGACCCGAC ACACGTGCTT
hinPI hpaII/snoI
bspl286
bsiHKAI
bmyI
apaLI/snoI
aluI
aluI
5001 CCCCCCGTTC AGCCCGACCG CTGCGGCTTA TCCGGTAACAT ATCGTCTTGA GTCCAACCGG GTAAGACAGG ACTTATCGCC ACTGGCAGCA GCCACTGGTA
GGGGGGCAAG TCGGGCTGGC GACGCGGAAT AGGCCATTTGA TAGCAGAACT CAGGTGCGG CATTCGTGTC TGAATAGCGG TGACCGTCTG CCGTGACCAT
fnu4HI alwNI[dcM-]
bsOFI fnu4HI
nspBII bsoFI
acilI hinPI mspI fnu4HI
mcrI bbvI bsaWI bsoFI
bsiEI hhaI/cfoI hpaII bbvI bsrI maeIII
5101 ACAGGATTAG CAGAGCCAGG TATGTAGGCG GTGCTACAGA GTTCTTGAAG TGTGGCCTA ACTACGGCTA CACTAGAAGG ACAGTATTG GTATCTGCGC
TGTCCTAATC GTCTCGCTCC ATACATCCGC CACGATGTCT CAAGAACTTC ACCACCGGAT TGATGCCGAT GTGATCTTCC TGTCAATAAC CATAGACGCG
mnII acilI scfI
bslI rmaI
haeIII/palI maeI
haeI bfaI
hinPI hhaI/cfoI

FIG. 41Q

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[illegible]

R141G.

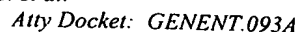


FIG. 41T



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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Appl. No.: 09/234,182

Atty Docket: GENENT.093A

```

nlaIII  hinPI
rcal    thal
bspHI   fndII/mvnl
        bstUI
        bsh1236I
        aciI
        nlaIV hhaI/cfoI
        bsmAI bsrBI
        6401 TTGCTCATG ACGGATACA TATTGAATG TATTAGAAA AATAACAAA TAGGGTTCC GGCACATTT CCCCAGAAAG TGCCACCTGA CGTCTAAGAA
AACAGAGTAC TGCCTATGT ATAAACTTAC ATAAATCTTT TTATTGTGTT ATCCCAAGG CGCGTGTAAG GGGGCTTTTC ACGGTGGACT GCAGATTCTT
        maeII
        hnlI/acyI
        ahaII/bsaHI
        aatII ddeI

sau96I
haeIII/palI
asuI      mboII
ecoO109I/draII
        mnlI      bpuAI
        bssSI      bbsI
        6501 ACCATTATTA TCATGACATT AACCTATATA AATAGGCGTA TCACGAGGCC CTTCCTCTTT CAA (SEQ ID NO.61)
TGGAATAAT AGTACTGTAA TTGGATATTT TTATCCGCAT AGTGCTCCGG GAAAGCAGAA GTT
        nlaIII
        rcal    tru9I
        bspHI   mseI
```

FIG. 41U



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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Atty Docket: GENENT.093A

>length: 6563

aatII(GACGTC): 1645 6489
acc65I(GGTACC): 403 823
accI(GTMKAC): 1093 1963 4449
accII(TCCGGA): 3867[dam-]
aciI(CCGC): 178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
see hinII
acyI 1307 4678
aflIII(ACRYGT): 1788
ageI(ACCGGT): 1645 1813 2616 2637 2751 3408 6107 6489
ahaII/bsaHI(GRCGYC): 5435 5454 6146
ahaII/draI(TTTAA): 346 5566
ahdI/eam1105I(GACNNNNNGTC): 72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
alulI(AGCT): 2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
5922
alw44I/snoI(GTGCAC): 1831 4494 4992 6238
alwI[dam-](GGATC): 412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
6196 6214
alwNI[dcn-](CAGNNNCTG): 1117 1385 5089
apaI(GGGCCC): 1695
apaLI/snoI(GTGCAC): 1831 4494 4992 6238
apoI(RAATTY): 1 391 4093
apyI[dcn+](CCWGG): 640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
aseI/asnI/vspI(ATTAAAT): 5742
asnI see aseI
asp700(GAANNNTTC): 905 930 4234 6166
asp718(GGTACC): 403 823
aspHI see hgiAI
aspi see tthIIII
asuI(GGNCC): 1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463

FIG. 41V



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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Stop Template Primer

SL.97.2 5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3' (SEQ ID NO.63)

NNS Randomization Primer

SL.97.3 5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3' (SEQ ID NO.64)

FIG. 42



Randomization of Position N35 of Variable Light Chain CDR-1
Amino Acid Frequency

Phage Display (NNS Codon Library) Sort #3

Amino Acid	Frequency	% Total	IC50 (nM)
Asparagine (wt)	1	5.6	4.9
Glycine	6	16.6	3.1
Aspartic Acid	3	16.6	3.1
Glutamic Acid	4	22.2	0.1
Alanine	2	5.6	0.2
Lysine	1	5.6	ND
Serine	1	1.9	ND

FIG. 43A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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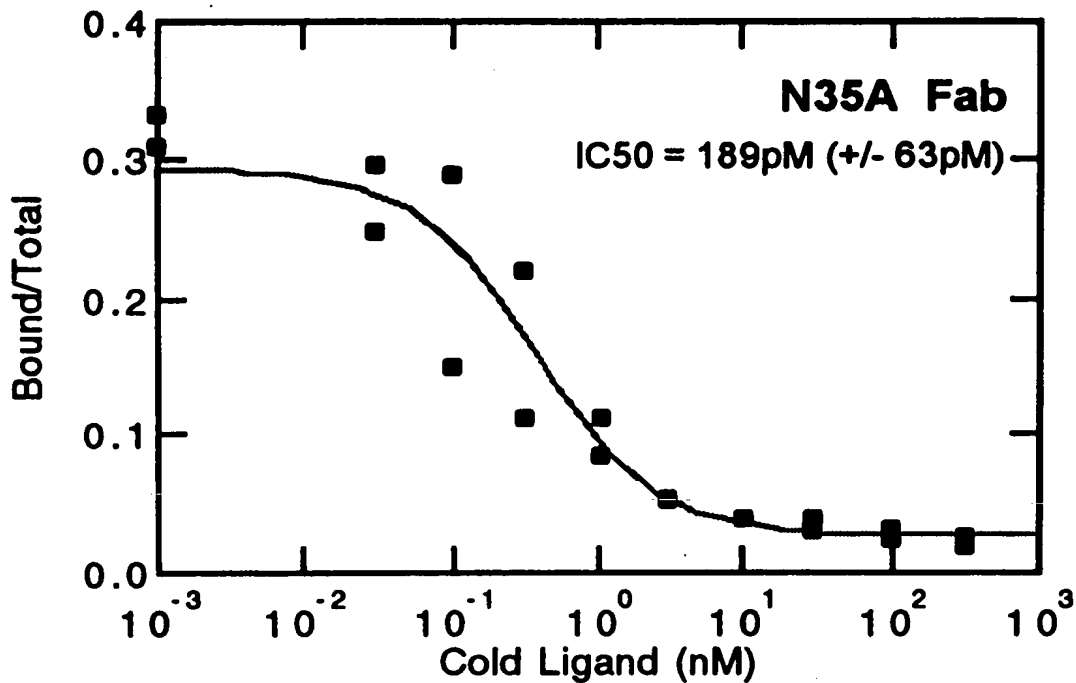


FIG. 43B

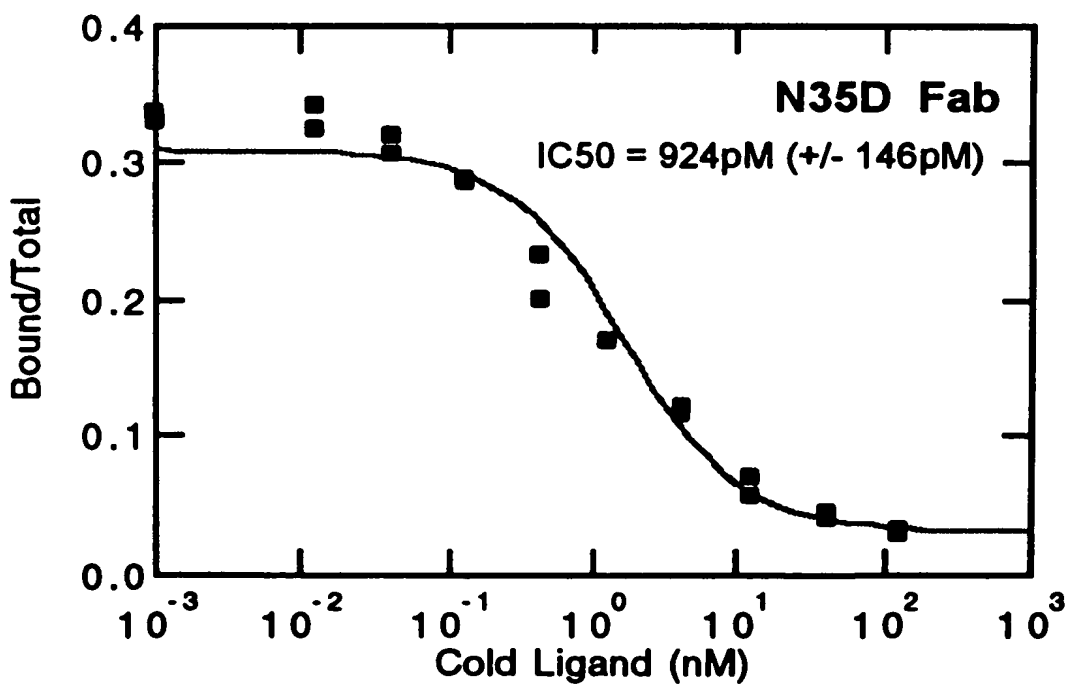


FIG. 43C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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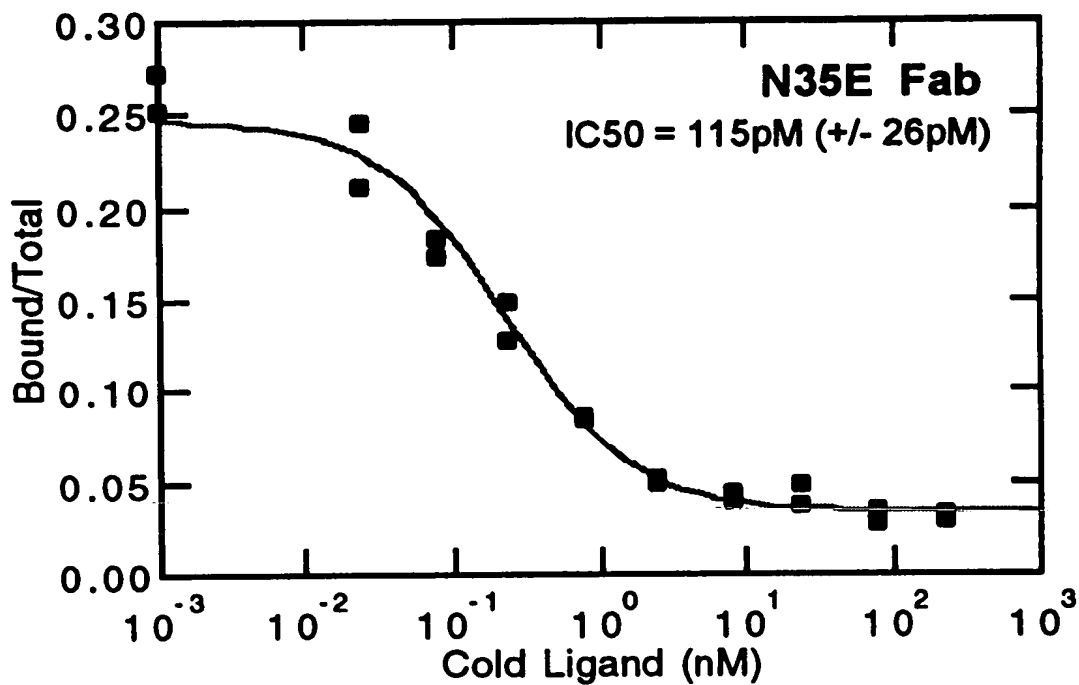


FIG. 43D

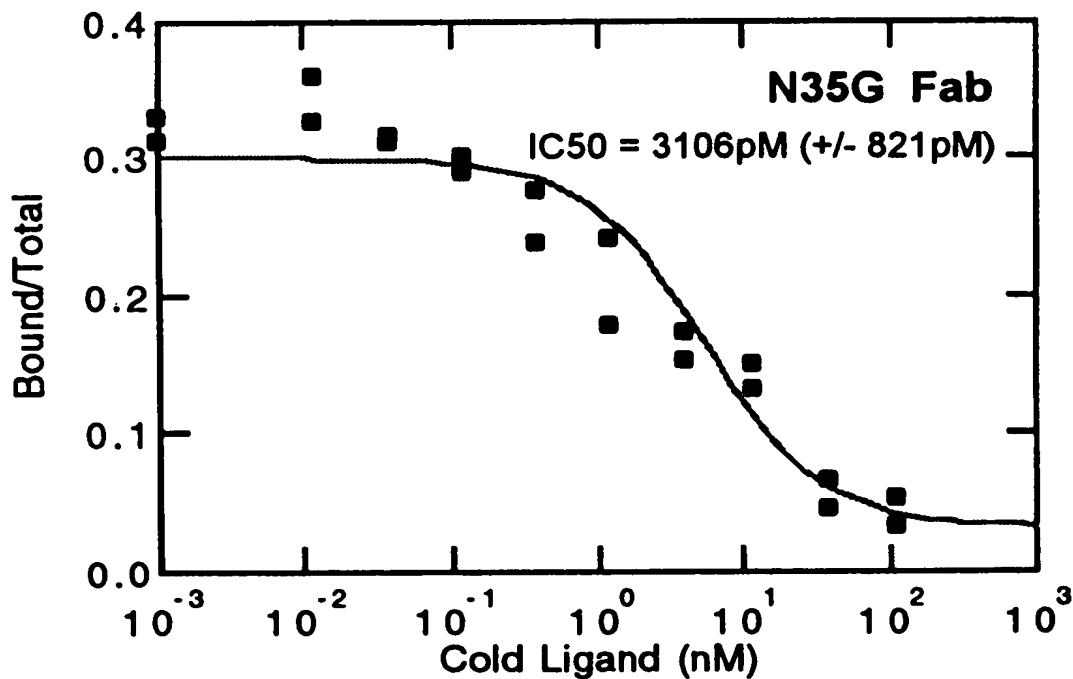


FIG. 43E

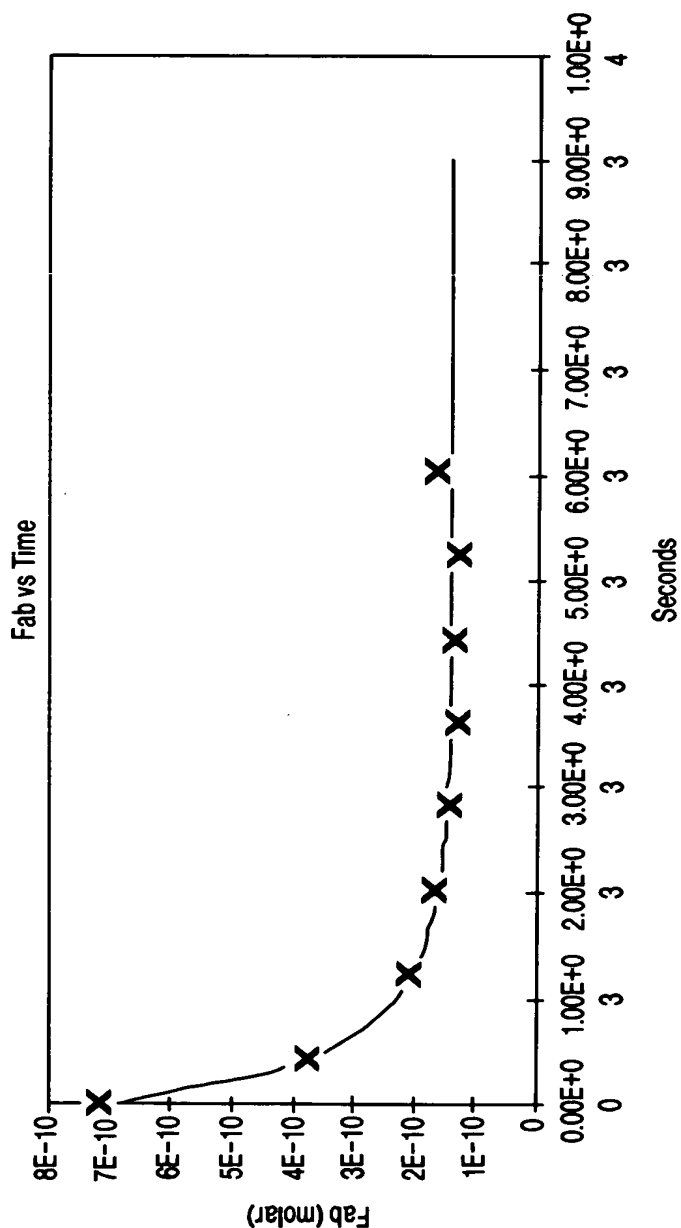


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')₂.

SAMPLE	ka	kd	Kd
6G4V11N35A-Fab	ND	ND	114pM
6G4V11N35A-F(ab') ₂	2.0x10 ⁶	2.1x10 ⁻⁴	109pM
6G4V11N35E-Fab	4.7x10 ⁶	2.6x10 ⁻⁴	54pM

FIG. 44



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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1 ATGAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGAGACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACTCTGCATA
18 R V T I T C R S S Q S L V H G I G E T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S O S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCTA CAGTGTCTCG TCCTGTCGTT CCTGTCGTGG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTTCTCGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TCGCGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.62)

(SEQ ID NO.65)

FIG. 45



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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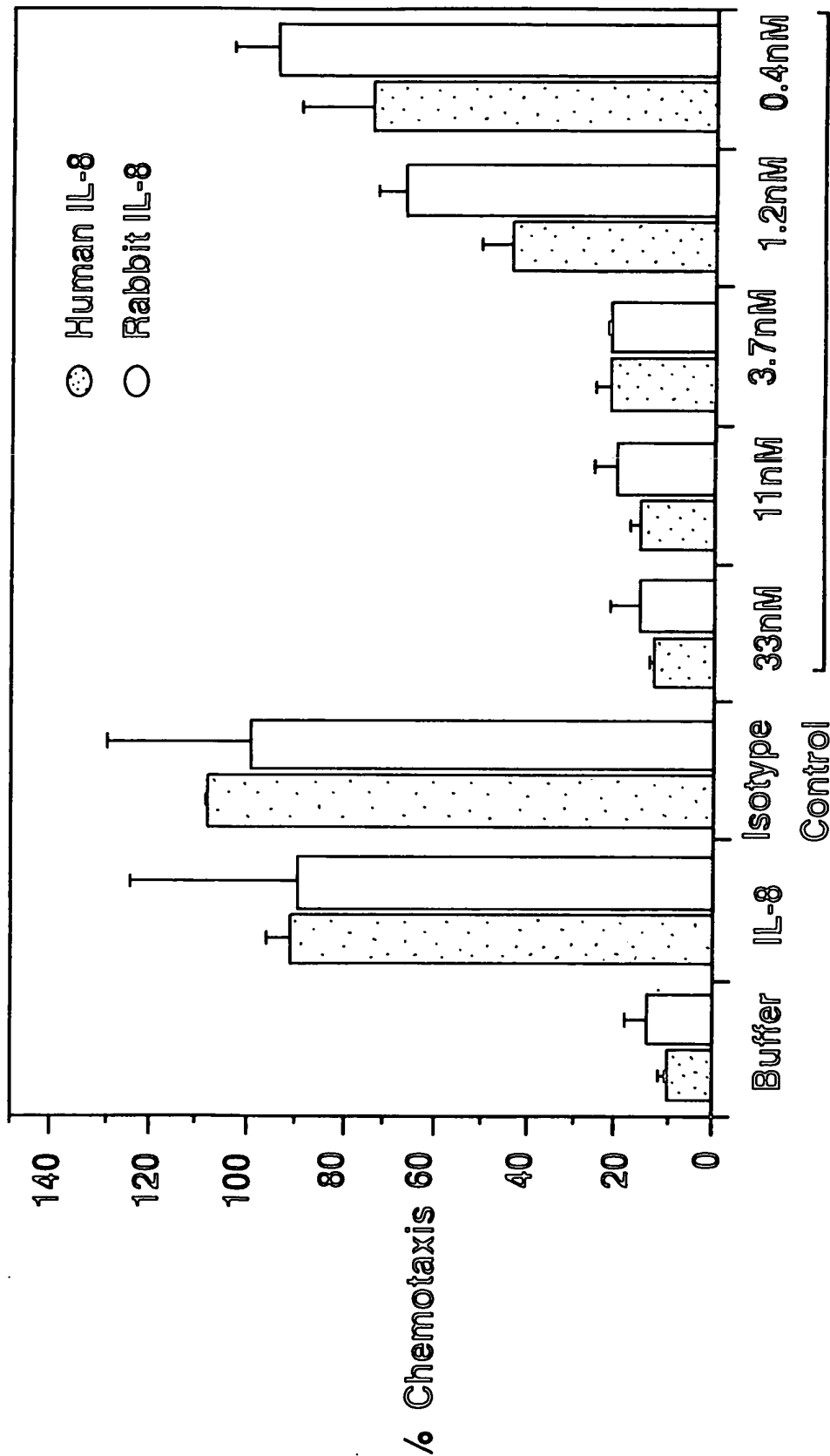


FIG. 46



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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Atty Docket: GENENT.093A

N35AH1upr

5'-CTAGTCAGTCTGGCGGTGGCCTGGTGCAGCCAGGGGGCTCACTCCGTTTGTCTGTGCAGCTTCTGGCTACTCCTTC-3'
(SEQ ID NO.66)

N35AH1wr

5'-TCGAGAGGAGTAGCCAGAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCGCCAGACTGCAC
AG-3' (SEQ ID NO.67)

Bold indicates nucleotide change destroying PvuII site.

FIG. 47



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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> length: 8120 (circular)
> This has the pSVI backbone with the PRK7 cloning linker (pSVI7) and the intron DHFR(ID)
> made from pSVI.WTSD.D by adding a linearization linker(1L) into the HpaI site

```

cac8I
aluI
sstI
sacI
hgiJII
hgiAI/aspHI
ec1136II
bsp1286
bsiHKAI
bmyI
banII
taqI
1 TTCGAGCTCG CCCGACATTG ATTATTGACT AGAGTCGATC GACAGCTGTG GAATGTGTGT CAGTTAGGTT GTGGAAGTC CCCAGGCTCC CCAGCAGGCA
NAGCTCGAGC GGGCTGTAC TAATACTGA TCTCAGCTAG CTGTCGACAC GTTACACACA GTCAATCCCA CACCTTTTTCAG GGTCCGAGG GGTCGTCGGT

scrFI mvaI ecorII dsav bstNI apyI[dcM+] bsaJI bsmFI nlaIV cac8I
sau3AI aluI mboI/ndeII[dam-] dpnI[dam+] pvuI/bspCI pleI dpnII[dam-] hinfI taqI[dam-] rmaI mcrI pvuII bseI nspBII bfaI taqI[dam-]
cac8I
ppu10I nsiI/avaIII nlaIII sphI nspI nspHI cac8I
scrFI mvaI ecorII dsav bstNI apyI[dcM+] bsaJI bsmFI nlaIV cac8I
sfani ppu10I nsiI/avaIII nlaIII sphI nspI nspHI cac8I
101 GAAGTATGCA AAGCATGCGT CTCAATTAGT CAGCAACCGAG GTGTGGAAG TCCCGAGGCT CCCGAGCAGG CAGAAGTATG CAAAGCATGC ATCTCAATTA
CTTCATACGT TTCGTACGTA GAGTTAATCA GTCGTTGGTC CACACCTTTC AGGGGTCCGA GGGGTCTGTC GTCTTCATAC GTTTCGTACG TAGAGTTAAT

acII foki bsmFI nlaIII styI ncoI bseI dsal acII bsaJI
acII acII acII bsrI acII
201 GTCAGCAACC ATAGTCCCGC CCTTAAGTCC GGCATCCCG CCCCTAACTC GCGCCAGTTC CGCCATTCT CCGCCCGCATG GCTGACTAAT TTTTTTATT
CAGTCGTTGG TATCAGGGCG GGGATTGAGG CGGGTAGGCG GGGGATTGAG GCGGTTCAAG GCGGGGTAC CGACTGATTA AAAAAATAA
```

FIG. 48A

[illegible]

FIG. 48B

```

scrFI
mvaI
ecorII
dsav
bstNI
tfII
hinfI
mboII
apyl[dcmt+]
sexAI
dclI mboII taqI
ahaiII/draI
tru9I
msei
mboII
earI/ksp632I
mnli
eco57I
mboII
earI/ksp632I
mnli
601 CAAAGAATGA CCACAACCTC TTCAGTGGAA GGTAACAGA ATCTGGTGAT TATGGGTAGG AAAACCTGGT TCTCCATTCC TGAGAGAAT CGACCTTTAA
GTTTCTTACT GGTGTTGGAG AAGTCACCTT CCATTTGTCT TAGACCACCTA ATACCATCC TTTTGGACCA AGAGGTAAGG ACTCTTCTTA GCTGGAATTT

sstI
sacI
hglII
hglAI/asphI
ecII36II
bsp1286
bsiHKAI
bmyI
mnli alul
mnli banII
bssSI
bslI bseRI
bstXI
fokI sfaNI msei
afII/bfrI
tru9I
msei
aseI/asnI/vspI
dclI
701 AGGACAGAAT TAATATAGTT CTCAGTAGAG AACTCAAGA ACCACACAGA GGAGCTCATTT TCTTTGCCAA AAGTTTGGAT GATGCCTTAA GACTTATTGA
TCCTGTCTTA ATTATATCAA GAGTCATCTC TTGAGTTTCT TGSTGGTGCT CCTCGAGTAA AAGAAGGTT TTCAAACCTA CTACGGAATT CTGAATAACT

haeIII/palI
haeI
scrFI
mvaI
ecorII
dsav
tfII
bstNI
nlaIII
apyl[dcmt+]
hinfI
apyl[dcmt+]
hinfI
pleI
dclI
mapI
hpaII
bsaWI
accI nlaIII
mnli
801 ACAACCGGAA TTGGCAAGTA AAGTAGACAT GGTITGGATA GTGGAGGCA GTTCTGTTTA CCAGGAAGCC ATGAATCAAC CAGGCCACCT TAGACTCTTT
TGTTGGCCTT AACCGTTTCAT TTTCATCTGTA CCAACCTAT CAGCCTCCGT CAAGACAAAT GGTCTCTCGG TACTTAGTTG GTCCGGTGA ATCTGAGAAA

```

FIG. 48C

[illegible]

```
scrFI
mvaI
corII
dsaV
bstNI
apyI[dcml]
sau96I
```

[illegible]

styI
 bsaJI
 sau3AI
 mboI/ndeII[dam-]
 dpnI[dam+]
 dpnII[dam-]
 alwI[dam-]
 bstYI/xhoII
 cac8I
 bsaJI
 nlaIII
 styI
 ncoI
 dsaI bsmFI
 ppu10I
 nslI/avaIII
 1101 ATGCATTTTT ATAAGACCAT GGCACTTTTG CTGGCTTTAG ATCCCTTTGG CTTGCTTTAGA ACGCAGCTAC AATTAAATACA TAACCTTTATG TATCATACAC
 TACGTAATAAAA TATTCTGGTA CCTGTAAAC GACCGAAATC TAGGGGAACC GAAGCAATCT TCGCTCGATG TTAATTATGT ATTGGAATAC ATAGTATGTG

sau96I
avaII
asuI
scrFI
mvaI
ecorII

FIG. 48D



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

1201 ATACGATTTA GGTGACACTA TAGATAACAT CCACCTTTGCC TTCTCTCTCCA CAGGTGTCCA CTCCAGGTC CAACTGCACC TCGGTTCTAT CGATGAATT
TATGCTAAAT CCACTGTGAT ATCTATTGTA GGTGAACCG AAGAGAGGT GTCCACAGGT GAGGTCCAG GTTACAGTGG AGCCAAGATA GCTTAAGTAA
seq from pRK6G425VH: Cla-AvrII⁺

1301 CCACCATGGG ATGGTCATGT ATCATCCTTT TTCTAGTAGC AACTGCAACT GGAGTACATT CAGAAGTTCA GCTAGTGCAG TCTGGCGGTG GCCTGGTGCA
GGTGGTACCC TACCAGTACA TAGTAGGAAA AAGATCATCG TTGACGTTGA CCTCATGTAA GTCTTCAACT CGATCAGTTC AGACCGCCAC CGGACCCAGT
E V Q L V Q S G G L V Q

1

1401 GCCAGGGGCG TCACTCCGTT TGTCCTGTGC AGCTTTCTGGC TACTCCTTCT CGAGTCACTA TATGACTGG GTCCGTGAGG CCCCAGGTAA GGGCCTGGAA
CGGTCCCGCG AGTGAGGCAA ACAGGACACG TCGAAGACCG ATGAGGAAGA GTCAGTGAT ATAGCTGACC CAGGCAGTCC GGGGCCCATTT CCGGACCTT
14 P G G S L R L S C A A S G Y S F S S H Y M H W V R Q A P G K G L E

FIG. 48E

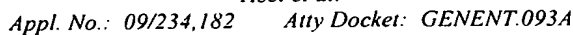


FIG. 48F



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

```
scrFI      hinPI      hgiAI/aspHI      mspI      hpaII      scfI
mvaI      nlaIV      bsp1286      bmyI      hpaII      scfI
ecorII      nari      bsiHKAI      cac8I      hpaII      scfI
econI      kasi      bmyI      hpaII      hpaII      scfI
dsav      hnlI/acyI      hpaII      hpaII      hpaII      scfI
bstNI      hgiCI      haeII      hpaII      hpaII      scfI
bslI      haeII      bani      hpaII      hpaII      scfI
apyI[dcM+]      bni      ahaII/bsaHI      aciI      apalI/snoI      dsav
fnu4HI      ahaII/bsaHI      ddel      hhaI/cfoI      nspBI      alw44I/snoI      cauII      scfI
bsOFI      ageI      tth111I/aspI      ddel      hhaI/cfoI      nspBI      alw44I/snoI      cauII      scfI
bbsI      ageI      tth111I/aspI      ddel      hhaI/cfoI      nspBI      alw44I/snoI      cauII      scfI
1801 CTGGCTGCC TGCTCAAGGA CTACTTCCCC GAACCGGTGA CGGTGCTGTG GAACCTCAGG CCGCTGACCA CCGGCGGTGCA CACCTTCCCG GCTGTCTCTAC
GACCCGACGG ACCAGTTCTT GATGAAGGGG CTGGGCCACT GCCACAGCAC CTTGAGTCCG CGGGACTGGT CGCCGCACT GTGGAAGGGC CGACAGGATG
147 L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q
bslI      ageI      tth111I/aspI      ddel      hhaI/cfoI      nspBI      alw44I/snoI      cauII      scfI
1801 CTGGCTGCC TGCTCAAGGA CTACTTCCCC GAACCGGTGA CGGTGCTGTG GAACCTCAGG CCGCTGACCA CCGGCGGTGCA CACCTTCCCG GCTGTCTCTAC
GACCCGACGG ACCAGTTCTT GATGAAGGGG CTGGGCCACT GCCACAGCAC CTTGAGTCCG CGGGACTGGT CGCCGCACT GTGGAAGGGC CGACAGGATG
147 L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q
fnu4HI      bsoFI      nlaIV      hgiCI      bni      hinfI
bsOFI      rmai      bsp1286      maeI      bni      hinfI
maeIII      bsp1286      maeI      bni      hinfI
hphI      bmyI      mnlI      bvi      bmyI      maeII
1801 AGTCCTCAGG ACTCTACTCC CTCAGCAGCG TGCTGACTGT GCCCTCTAGC AGCTTGGGCA CCGACACCTA CATCTGCAAC GTGAATCACA AGCCACGAA
TCAGGAGTCC TGAGATGAGG GAGTCGTCCG ACCACTGACA CCGGAGATCG TCGAACCGGT GGTCTGGAT GTAGACGTG CACTAGTGT TCGGGTCGTT
181 S S G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N
ahdI/eam1105I
sau96I
avaII
scrFI      mvaI      asuI
mvaI      ecorII      dsav
bstNI      nlaIV      mboII
bsaJI      bsmFI      bpuAI
apyI[dcM+]      bbsI      mnlI
2001 CACCAAGGTG GACAAGAAAG TTGAGGCCAA ATCTTGTGAC AAAACTCACA CATGCCACC GTGCCAGCA CCGTGAACCTCC TGGGGGACC GTCAGTCTTC
GTGGTTCCAC CTGTTCTTTC AACTCGGTT TAGAACACATG TTTTGTGTGT GTACGGGTG CACGGGTG CACCCCTGG ACCCCCTGG CAGTCAGAAG
214 T K V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F
```

FIG. 48G



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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```
sau96I
nlaIV
mspI
hpaII
scrFI
ncII
dsav
sau3AI avall nlaIII
mboI/ndeII[dam-] nspI
nlaIII cauII mnII nspHI
rcal dpnII[dam+] ddel mslI
mnII dpnII[dam-] eco8II maeIII
styI mnII bspHI[dam-] asuI bsu36I/mstII/sauI maeII
earI/kap632I bsaJI mslI bspHI[dam-] GGACCCCTGA GGTACATGC GTGGTGGTGG ACGTGAGCCA CGAGACCCCT GAGGTCAAGT
2101 CTCTTCCCC CAAACCCAA GGACACCTC ATGATCTCCC GGACCCCTGA GGTACATGC GTGGTGGTGG ACGTGAGCCA CGAGACCCCT GAGGTCAAGT
GAGAAGGGG GTTTGGTT CCTGTGGAG TACTAGAGG CCTGGGACT CAGTGTCAG CACCACCACC TGCACCTCGT GCTTCTGGGA CTCCAGTTCA
247 L F P P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F
acII
thai
fnuDI/mvnl
bstUI
bsh1236I
sacII/sstII
nspBI
kspI
dsal
bsaJI
maeII
rsal
csp6I
fnu4HI mnII rsal maeII bsaAI
bsaJI bseRI csp6I bsaAI
2201 TCAACTGTA CGTGGACGGC GTGGAGTGC ATAATGCCAA GACAAGCCG CGGAGGAGC AGTACAACAG CAGGTACCGT GTGGTCAGCG TCCTCACCGT
AGTTGACCAT GCACCTGCCG CACCTCCAGC TATTACGGT CTGTTTCGGC GGCCTCCTCG TCATCTGTC GTGCATGGCA CACCAGTCGC AGGAGTGCA
281 N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V
scrFI
mvaI
ecorII
dsav
ecoNI bstNI bsrI
bsLI apyI[dcn+]
2301 CCTGACCCAG GACTGGCTGA ATGGCAAGGA GTACAAAGTC AAGGTCTCCA ACAAGCCCT CCAGCCCCC ATCGAGAAA CCATCTCCA AGCCAAAGG
GGACGTGGTC CTGACCGACT TACCGTCTCT CATGTTCAAG TTCCAGAGT TGTTCGGGA GGTTCGGGG TAGCTCTTTT GGTAGAGTT TCGGTTTCCC
314 L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G
fnu4HI bsoFI
bbvI
bsoFI
```

FIG. 48H

```

scrFI
ncII
mspI
hpaII
dsav
cauII
xmaI/pspAI
smaI
scrFI
ncII
dsav
cauII
fokI
rsal
csp6I
bslI bsaJI mboII
bspl407I/bsrGI bslI avai earI/ksp632I
avaI
2401 CAGCCCGGAG AACCACAGGT GTACACCTGT CCCCCATCCC GGAAGAGAT GACCAAGAAC CAGGTCAGCC TGACCTGCCCT GGTCAAAGGC TTCTATCCCA
GTCGGGCTC TTGGTGTCCA CATGTGGGAC GGGGTAGGG CCCCTCTCTA CTGGTTCTTG GTCCAGTCGG ACTGGACGGA CCAGTTCCG AGATAGGGT
347 Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S
mspI
hpaII
fnu4HI
bsoFI
bsvI
bsrDI
bsaJI
malI bsaJI
dsal
bslI
2501 GCGACATCGC CGTGGAGTGG GAGAGCAATG GCGAGCCGGA GAACAACTAC AAGACCACGC CTCCCCTGCT GGACTCCGAC GGCTCCTTCT TCCTCTACAG
CGCTGTAGCG GCACCTCACC CTCTCGTTAC CCGTCGGCCT CTGTGTGATG TTCTGTGTCG GAGGCGACGA CCTGAGGCTG CCGAGGAAGA AGGAGATGTC
381 D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S
mboII
bpuAI
maeII
fnu4HI
bsoFI
bbvI
bspMI
bsaJI
aluI bsaJI
hphI
dsal
414 K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L

```

FIG. 48I



FIG. 48J

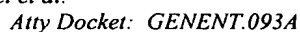


FIG. 48K



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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```

3501 CCACCTTTTC TTTTCTCCA CAGGTGTCCA CTCACAGGTC CAACCTGCACC TCGGTTCCGG AAGCTAGCTT GGGCTGCATC GATTGAATTC CACCATGGGA
GGTGAAAAAG AAAAGAGGT GTCCACAGGT GAGGTCCAG GTTGACGTGG AGCCAAGCGC TTGCATCGAA CCCGACGTAG CTAACCTAAG GTGGTACCTT
^cloning linker

3601 TGGTCATGTA TCATCCTTTT TCTAGTAGCA ACTGCAACTG GAGTACATTC AGATATCCAG ATGACCCAGT CCGCAGCTC CCTGTCCGCC TGTGTGGCG
ACCAGTACAT AGTAGGAAA AGATCATCGT TGACGTTGAC CTCATGTAAG TCTATAGGTC TACTGGGTCA GGGCTCGAG GGACAGCGG AGACACCCGC
1
18 R V T I T C R S S Q S L V H G I G A T Y L H W Y Q Q K P G K A P K

3701 ATAGGGTCAC CATCACTGC AGGTCAAGTC AAAGCTTAGT ACATGGTATA GGTGCTACGT ATTTACACTG GTATCAACAG AAACCGAGAA AAGTCCGAA
TATCCAGTG GTAGTGACG TCCAGTTGAG TTTTCAATCA TGTACCATAT CCAGCATGCA TAAATGTGAC CATAGTTGTC TTTGGTCTT TTGAGGCTT
18 R V T I T C R S S Q S L V H G I G A T Y L H W Y Q Q K P G K A P K
```

FIG. 48M



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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```

rsal          mnli          maelIII bsaJI          maelIII          fnu4HI
csp6I         bslI         maelIII bsaJI          maelIII          ddel bsoFI
4101 AGTACAGTGG AAGGTGGATA ACGCCCTCCA ATCGGCTAAC TCCCGGAGGA GTGTACACAGA GCAGGACAGC AAGGACAGCA CCTACAGCCT CAGCAGCACC
TCATGTCACC TTCCACTAT TCGGGAGGT TAGCCCATTT AGGGTCCTCT CACAGTGTCT CAGTGTCTGT CGTCTGTCTG TTCCTGTCTG GGATGTCGA GTCGTCTGCG
151 V Q W K V D N A L Q S G N S Q E S V T E Q D S K D S T Y S L S S T

scrFI         mval         ecorII        dsav          bstNI         apyI[dcM+]          maelIII
mval          ecorII        dsav          bstNI         apyI[dcM+]          maelIII
4201 CTGACGCTGA GCAAGCAGA CTACGAGAGA CACAAAGTCT ACGCCTGCGA AGTCAACCAT CAGGCGCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGGG
GACTGCGACT CGTTCTGCTT GATGCTCTTT GTGTTTCAGA TCGCGACGCT TCAGTGGGTA GTCCCGGACT CGAGCGGCA GTGTTCTCG AAGTTGTCGC
184 L T L S K A D Y E K H K V Y A C E V T H Q G L S S P V T K S F N R G

dcl          cellI/espI    blpI/bpul102I          hgal          accI          cac8I          maelIII          hphI          eco0109I/draII          maelIII          aluI
cellI/espI    blpI/bpul102I          hgal          accI          cac8I          maelIII          hphI          eco0109I/draII          maelIII          aluI
4201 CTGACGCTGA GCAAGCAGA CTACGAGAGA CACAAAGTCT ACGCCTGCGA AGTCAACCAT CAGGCGCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGGG
GACTGCGACT CGTTCTGCTT GATGCTCTTT GTGTTTCAGA TCGCGACGCT TCAGTGGGTA GTCCCGGACT CGAGCGGCA GTGTTCTCG AAGTTGTCGC
184 L T L S K A D Y E K H K V Y A C E V T H Q G L S S P V T K S F N R G

sau96I        aciI          haeIII/palI          fnu4HI          asuI          bsoFI          nlaIII          sfil          styl          aluI          haeIII/palI          fnu4HI          bsoFI          bbvI          maelIII          sfanI          apoI
aciI          haeIII/palI          fnu4HI          asuI          bsoFI          nlaIII          sfil          styl          aluI          haeIII/palI          fnu4HI          bsoFI          bbvI          maelIII          sfanI          apoI
4301 GAGAGTGTGA AGCTTGCGG CCAATGGCCCA ACTTGTTTAT TGCAGCTTAT AATGTTTACA AATAAGCAA TAGCATCACA AATTTCACAA ATAAGCATT
CTCTACAAT TGAACCGGC GGTACCGGT TGAACAATA ACATGCAATA TTACCAATGT TTATTTCTGT ATCGTAGTGT TTAAGTGT TATTTCGTAA
218 E C O (SEQ ID NO.72)
```

FIG. 480

FIG. 48P



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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```

sau3AI
mboI/ndeII(dam-)
dpmI(dam+)
sau96I
haeIII/palI
asul
dpmII(dam-)
pnuI/bspCI
mnlI acII
mboII cac8I
earI/ksp632I bslEI
CGAAGAGGCC CGCACCAGTC GGCCTTCCCA ACAGTTGCGT
CGGTGGCTAG CCGGAAGGGT TGTCAACGCCA
5001 TGGCGTTACC CAACCTTAATC GCCTTGACG ACATCCCCC TTCCGCCAGCT GCGGTAATAG
ACCGCAATGG GTTGAATTAG CCGAACGTCG TGTAGGGGGG AAGCGGTCGA CCGCATTATC
cac8I
aluI
pvuII
nspBII
cac8I
fokI
fnu4HI
bsoFI
bbvI
tru9I
msei
maeIII
5101 AGCCTGAATG CGGAATGGCG CCTGATGCGG TATTTTCTCC TTACGCATCT GTGCGGTATT TCACACCGCA TAGGTCAAAG CAACCATAGT ACGCGCCCTG
TCGGACTTAC CGCTTACCG GGACTACGCC GGACTACGCC ATAAAGAGG AATGGTAGA CACGCCATAA AGTGTGGCGT ATGCAGTTTC GTTGGTATCA TGC CGCGGGAC
hinPI
hhaI/cfoI
nlaIV
narI
kasi
hinII/acyI
hglCI
haeII
banI
bglI
ahaII/bseHI
5201 TAGCGGGGCA TTAAGCGCGG CGGGTGTGGT GGTACACTGC CAGCGCCCTA GCGCGCGCTC CTTTCGCTTT CTTCCTCTCC
ATCGCGCGT AATTCGCGC GCCACACCA CCAATGGCG TCGCACTGC GATGTGAACG GTCGGGGAT CCGCGGGGAG GAAAGCGAAA GAAGGAAGG
maeIII bbvI maeIII cac8I bfaI cac8I
mboII

```

FIG. 48R

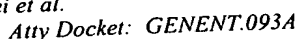


FIG. 48S

6201
bssSI maeIII taqI alwI[dam-] aciI bstYI/xhoII mboII
CACGAGTGG TTACATCGAA CTGGATCTCA ACAGCGGTAA GATCCTTGAG AGTTTTCGCC CCGAAGAAGG TTTTCCAATG ATGAGCAGCTT TTAAGTTCT
GTGCTCACCC AATGTAGCTT GACCTAGAGT TGTCGCCATT CTAGGAACCTC TCAAGAAGCGG GGTCTCTTGC AAAAGTTTAC TACTCGTGAA AATTTCACGA

6301
GCTATGTGGC GCGGTATTAT CCGGTGATGA CGCCGGGCAA GAGCAACTCG GTCCCGGCAT ACACATATCT CAGAATGACT TGGTTGAGTA CTCACCAAGTC
CGATACACCG CGCCATAATA GGCACACTACT CGGCCCGGTT CTGCTTGAGC CAGCGCGGTA TGTGATAAGA GTCTTACTGA ACCAACTCAT GAGTGGTCA

6401
ACAGAAAGC ATCTTACGGA GTAGAGAAAT TATGACAGTGC TGCCATAACC ATGAGTGATA ACACCTGGGC CAACCTACTT CTGACACAGA
TGTCTTTTCG TAGAATGCCT ACCGTACTGT CATCTCTCTTA ATACGTCAGC ACGTATTGG TACTCACTAT TGTGACGCCG GTTGAATGAA GACTGTTGCT

6501
TCGGAGGACC GAAGGAGCTA ACGCTTTTT TGCACAACAT CGGGGATCAT GTAACTCGCC TTGATCGCTG GGAACCGGAG CTGAATGAAG CCATACCAAA
AGCCTCTGCTG CTTCCTCGAT TGCGGAAAAA ACGTGTGTGA CCCCCTAGTA CATTGAGCGG AACTAGCAAC CCTTGGGCTC GACTTACTTC GGTATGTTT

FIG. 48U



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A

6601 CGACGAGGGT GACACCACGA TGGCAGCAGC AATGGCAACA ACGTTCCGCA AACTATTAACT TGGCGAACA CTACTCTAG CTTCCCGGCA ACAATTATA
GCTGCTCGCA CTCTGGTCTG ACGTCTGCTG TTAACGCTGT TGAACGCTGT TGAATAATG ACCGCTTGAT GAATGAGATC GAAGGCGCGT TGTAAATTAT

6701 GACTGGATGG AGCGGGATAA AGTTGCAGGA CCACTTCTGC GCTCGGCCCT TCCGGCTGGC TGGTTTATTG CTGATAAATC TGGAGCCGGT GAGCGTGGGT
CTGACCTACC TCGCCTATT TCAACGCTCT GGTGAAGACG CGAGCGGGA AGGCGGACCG ACCAATAAC GACTATTAG ACCTCGGCCA CTGCAACCCA

6801 CTCGCGGTAT CATTCAGCA CTTGGGCCAG ATGGTAAGCC CTCCGTATC GTAGTTATCT ACACGACGG GAGTCAGG ACTATGGATG AACGAATAG
GAGCGCATA GTAACGCTCT GACCCCGGTC TACCATTGG GAGGCGATG CATCAATAGA TGTGCTGCC CTCAGTCCGT TGATACCTAC TTGCTTTATC

6901 ACAGATCGCT GAGATAGGTG CCTCACTGAT TAAGCATTTG TAACTGTGAC ACCAAGTTA CTCATATATA CTTTAGATTG ATTTAAACT TCATTTTAA
TGCTAGCGA CTCTATCCAC GGAGTGACTA ATTGTAACC ATTGACAGTC TGGTTCAAAT GAGTATATAT GAAATCTAAC TAAATTTTGA AGTAAAAATT

7001 TTTAAAGGA TCTAGGTGAA GATCCTTTT GATAATCTCA TGACCAAAAT CCCTTAACGT GAGTTTCTCT TCCACTGAGC GTCAGACCCC GTAGAAAAGA
AAATTTCTCT AGATCCACTT CTAGAAAAA CTATTAGAT ACTGGTTTGA GGAATTTGA CTCAAAAGCA AGGTGACTCG CAGTCTGGG CATCTTTCT

FIG. 48V

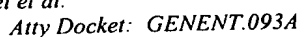


FIG. 48W

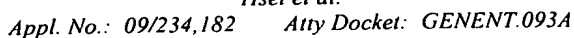


FIG. 48X



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```
thai
fnuDII/mvni
bstUI
bsh1236I
hinPI
hhaI/cfoI
thai
fnuDII/mvni          cac8I
bstUI haeIII/palI    aluI
bsh1236I             tru9I pvuII
mnlI eaeI tfII aseI/asnI/vsPI
aciI cfrI hinPI msel nspBII
7901 CCGGCTCTCC CCGGGCGTTG GCGGATTTCAT TAATCCAGCT GGCACGACAG GTTTCGCCGAC TGGAAAGCGG GCACTGAGCG CAACGCCAATT AATGTGAGTT
GGCGGAGAGG GCGCGGCAAC CGGCTAAGTA ATTAGTCA GCGTGCTGTC CAAGGGGCTG ACCTTTCGCC CGTCACTCGC GTTGGCGTTAA TTCACTCAA
tru9I msel maeIII
hinPI hhaI/cfoI aseI/asnI/vsPI
cac8I aciI bsrI
bsrI bsrI
mspI hpaII aciI
nlaIV bstNI          bsrBI aluI
hgICI apyI(dcm+)
bani bsaJI
8001 ACCTCACTCA TTAGGCACCC CAGGCTTTAC ACTTTATGCT TCCGGCTCGT ATGTTGTGTG GAATTGTGAG CGGATAACAA TTTCACACAG GAAACAGCTA
TGGAGTGAGT AATCCGTGGG GTCCGAAATG TGAATACGA AGGCCGAGCA TACACACAC CTTAACACTC GCCTATTGTT AAAGTGTC CTTTGTCTGAT
```

FIG. 48Y



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

```
tru9I
mseI
aseI/asnI/vspI
xmni
nlaiII asp700
8101 TGACCATGAT TACGAATTAA (SEQ ID NO.68)
ACTGGTACTA ATGCTTAATT

>length: 8120

aatII(GACGTC): 1690 5947
acc65I(GGTACC): 2969 3967 4529
accI(GTMRAC): 823 1039 2738 4237
acII(CCGC): 217 229 238 250 260 271 317 422 454 485 574 1385 1795 1871 2248 2250 2758 2982
3167 3179 3188 3200 3210 3221 3267 3372 3404 3449 3686 3949 4021 4318 4542 4727
4739 4748 4760 4770 4781 4827 4910 4914 5070 5127 5153 5166 5203 5217 5220 5248
5275 5680 5699 5741 5751 5790 5979 6026 6125 6234 6311 6355 6476 6522 6713 6804
7166 7175 7310 7420 7541 7560 7687 7715 7806 7827 7834 7877 7901 7911 7967 8070

see hinI
acyI
afIIII/bfRI(CTTAAG): 786
afIIII(ACRYGT): 932 7758
ageI(ACCGGT): 1833
ahaII/bsaHI(GRCGYC): 988 1690 1858 5117 5947 6329
ahaII/draI(TTTAAA): 696 4935 6290 6982 7001
ahdI/eamII05I(GACNNNNNGTC): 2087 6865
alul(AGCT): 5 44 332 386 390 753 1097 1165 1370 1431 1951 2603 2751 2784 3282 3336 3340
3562 3566 3676 3733 3792 4270 4288 4311 4344 4554 4842 4896 4954 5047 5333 5590
5803 5822 6516 6579 6679 7200 7457 7593 7819 7937 8096
alw44I/snoI(GTGCAC): 1876 5651 6198 7444
```

FIG. 48Z



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

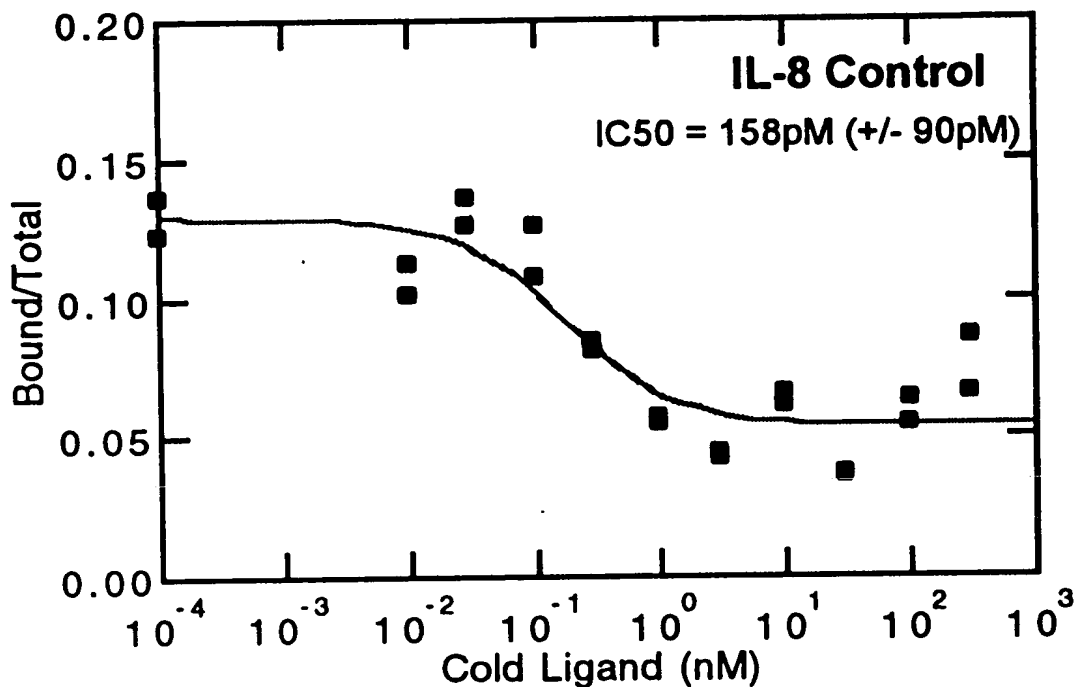


FIG. 49A

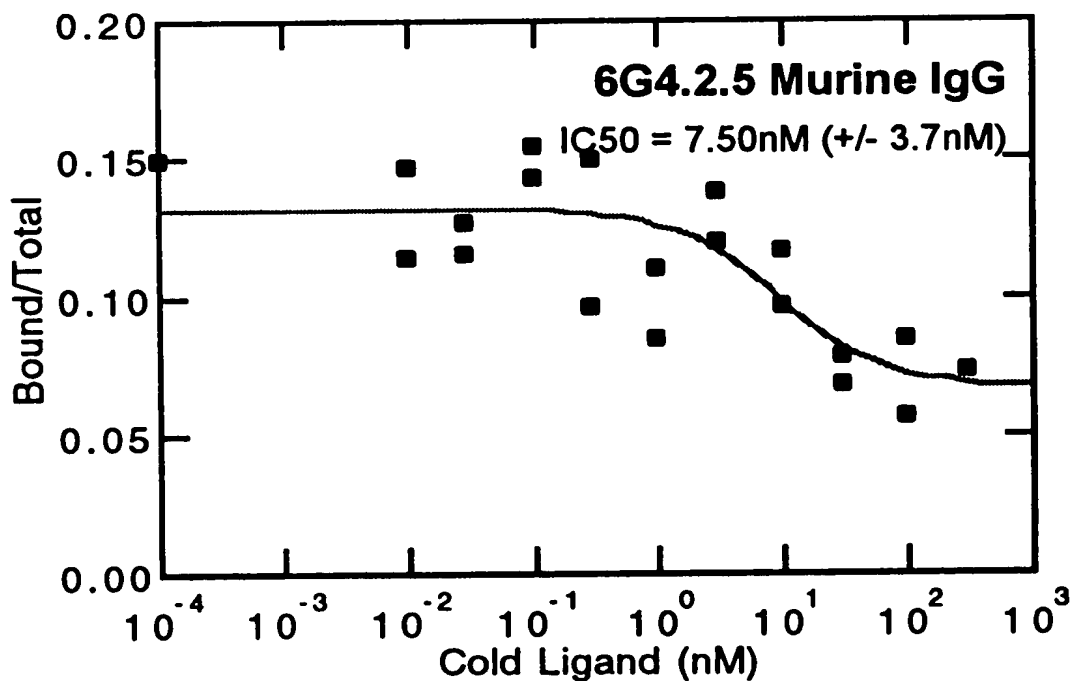


FIG. 49B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

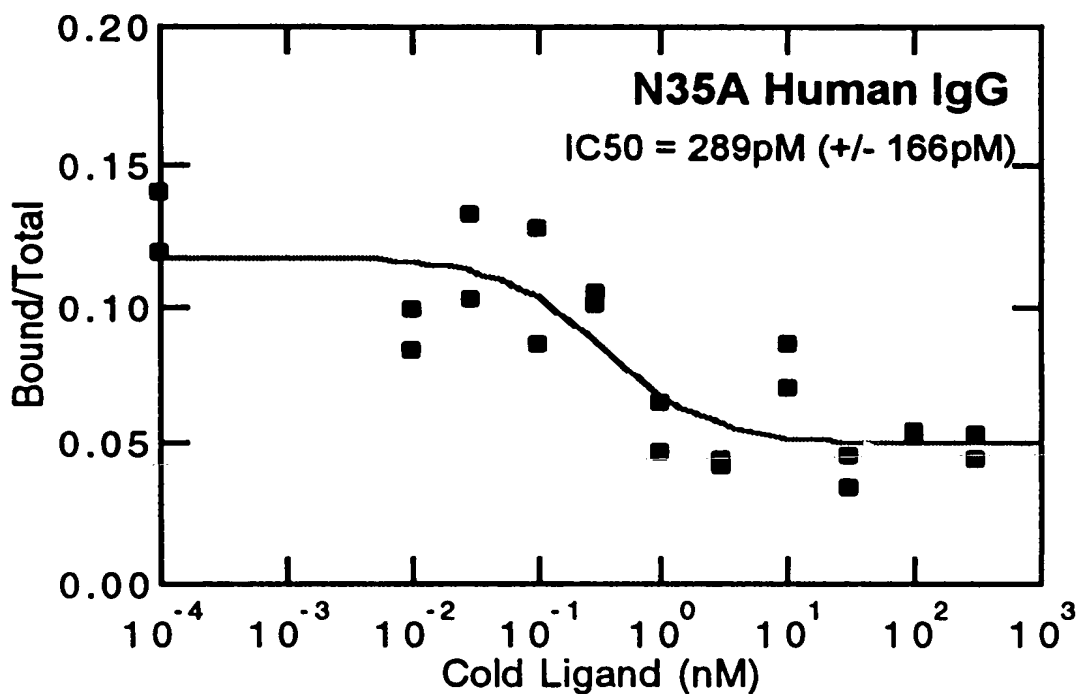


FIG. 49C

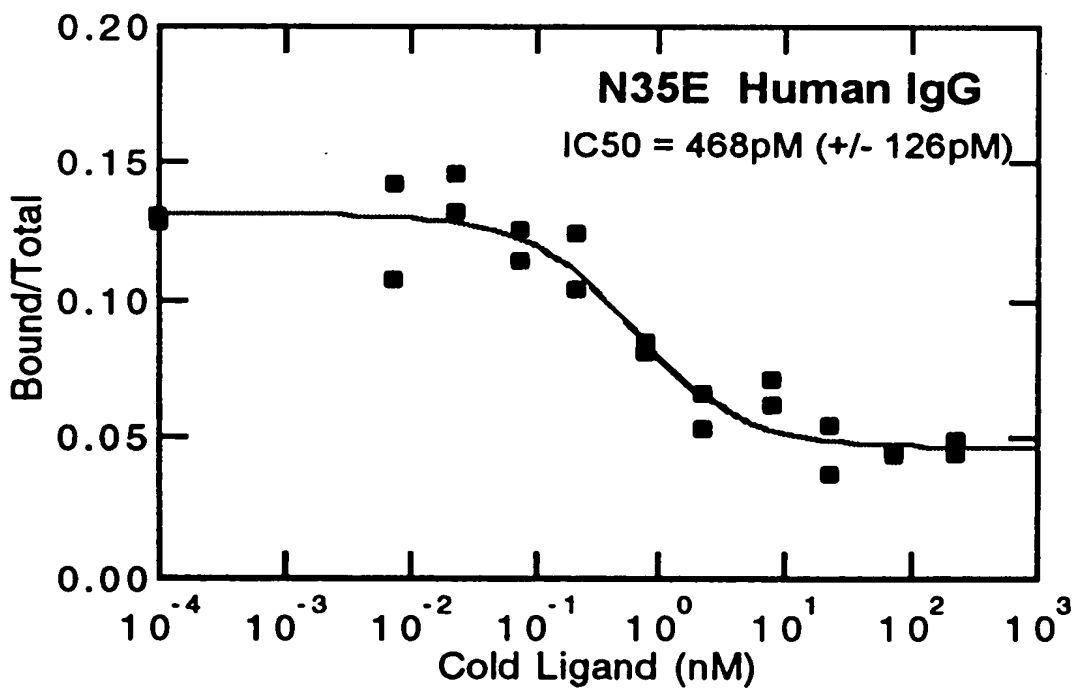


FIG. 49D



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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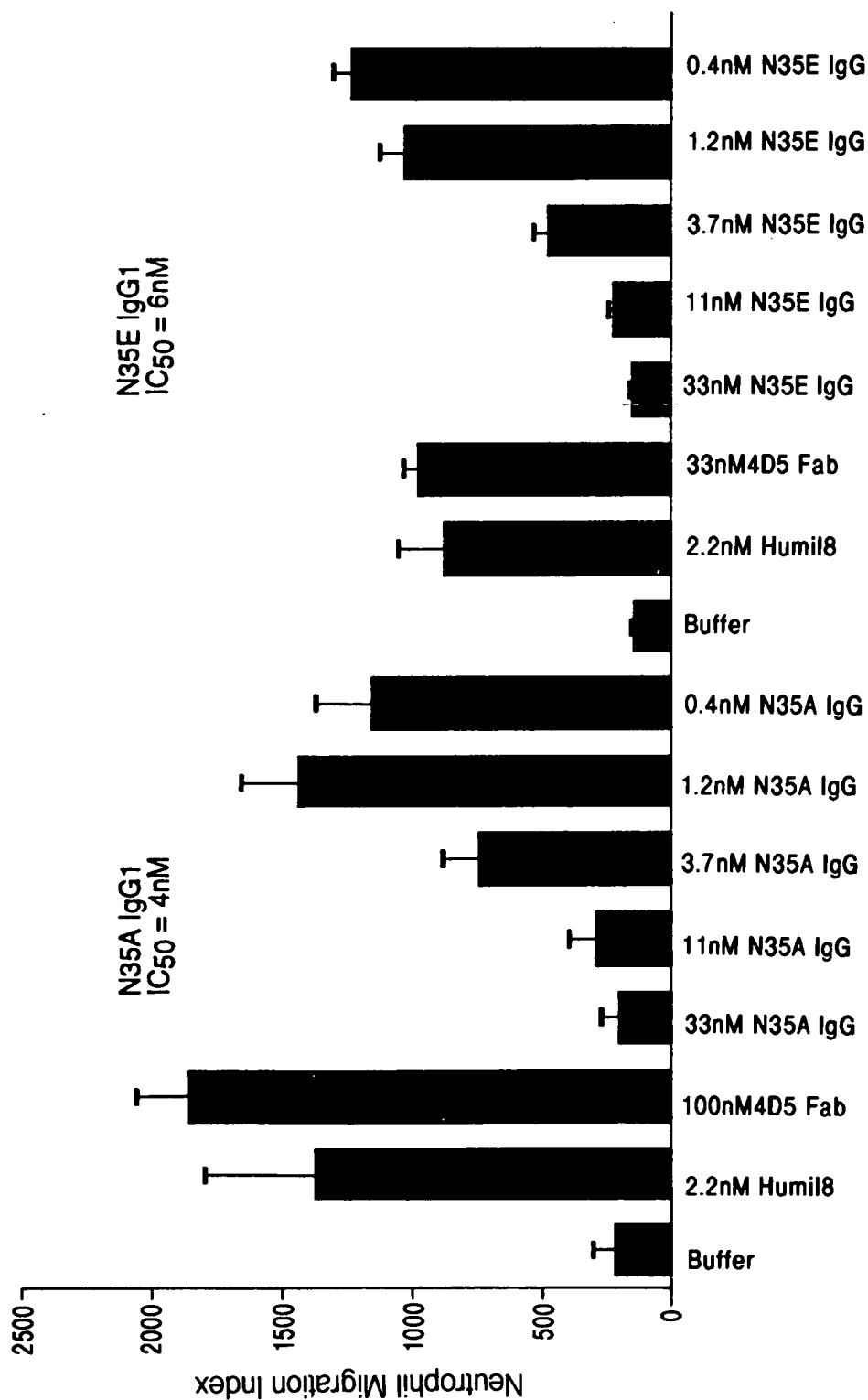


FIG. 50A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

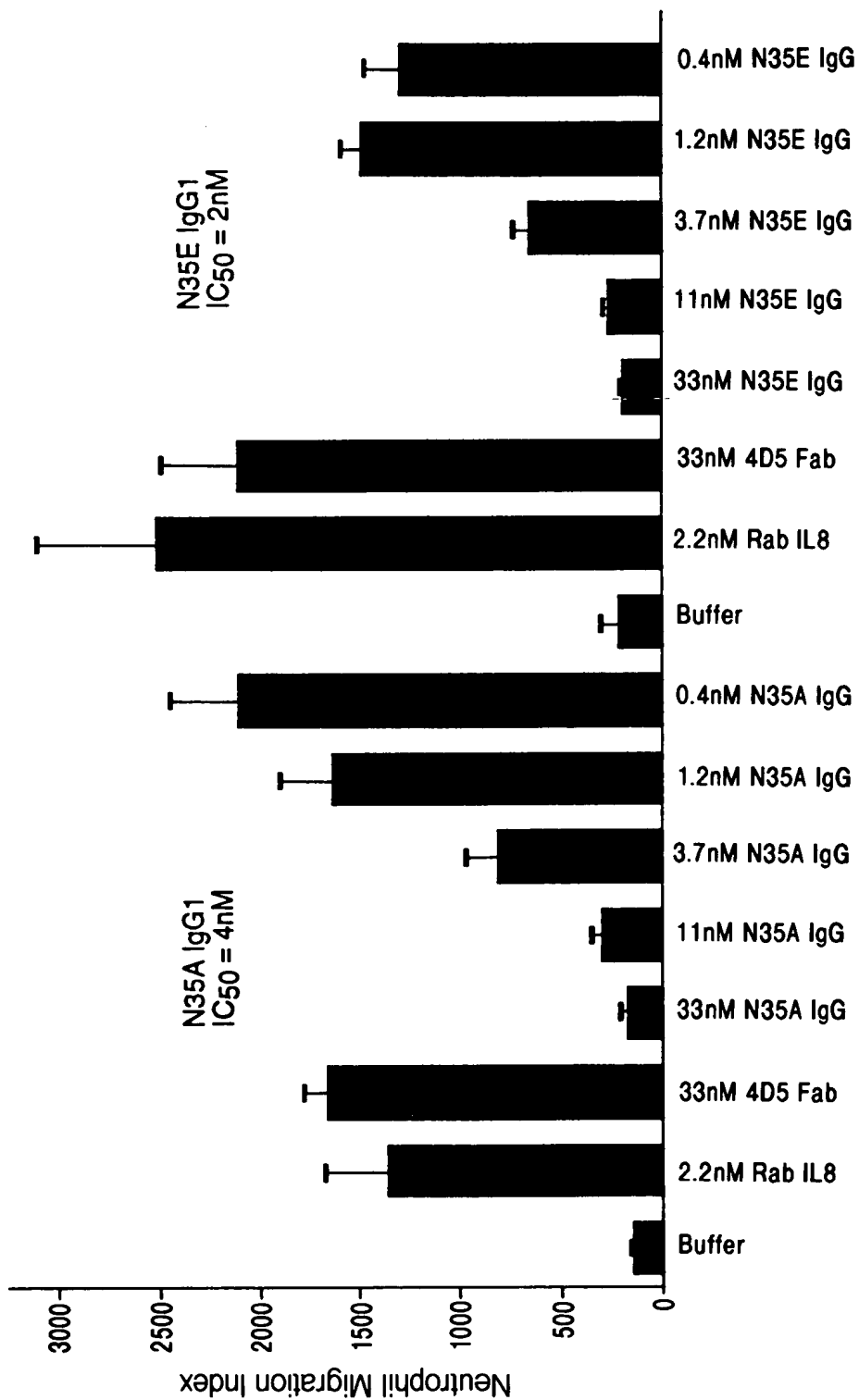


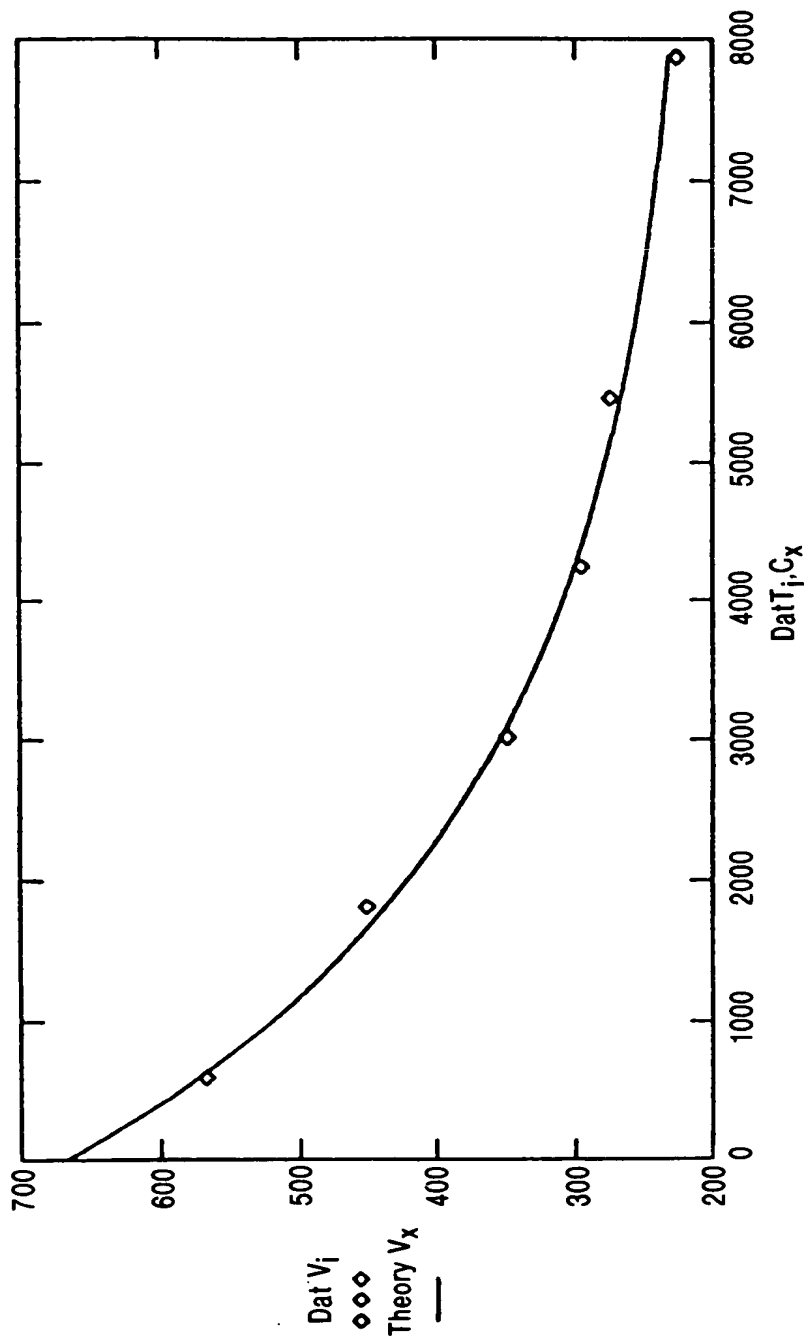
FIG. 50B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.IgG1

SAMPLE	k_a	k_d	K_d
Murine 6G4.2.5 IgG2a	8.3×10^5	2.9×10^{-4}	350pM
6G4V11N35A-IgG1	8.7×10^5	7.7×10^{-5}	88pM
6G4V11N35E-IgG1	3.0×10^6	1.4×10^{-4}	49pM

FIG. 51



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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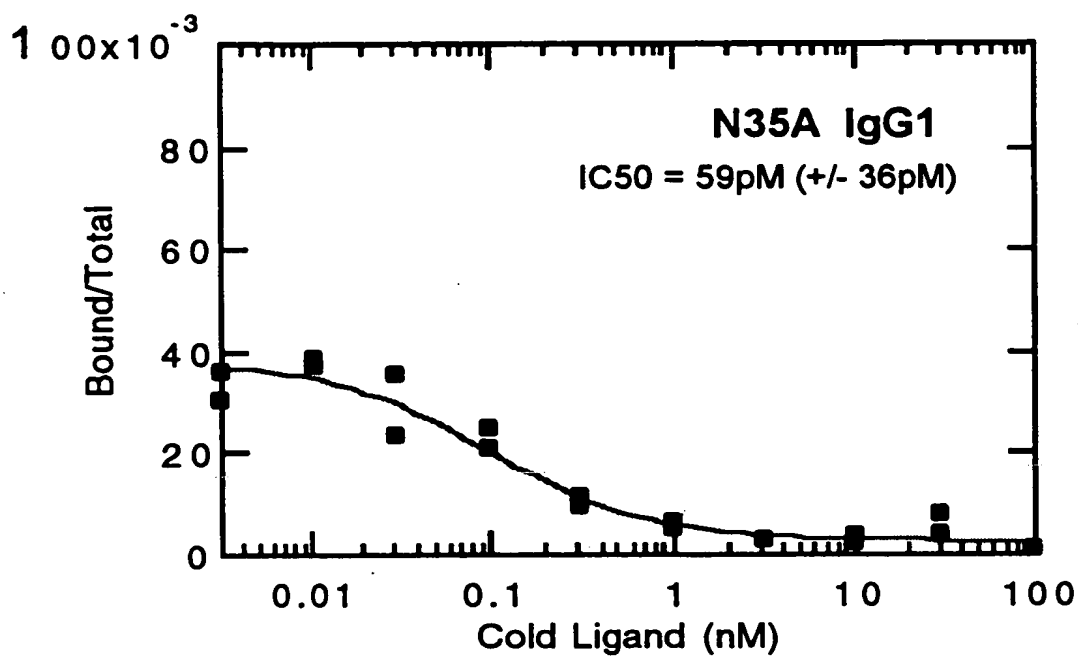


FIG. 52A

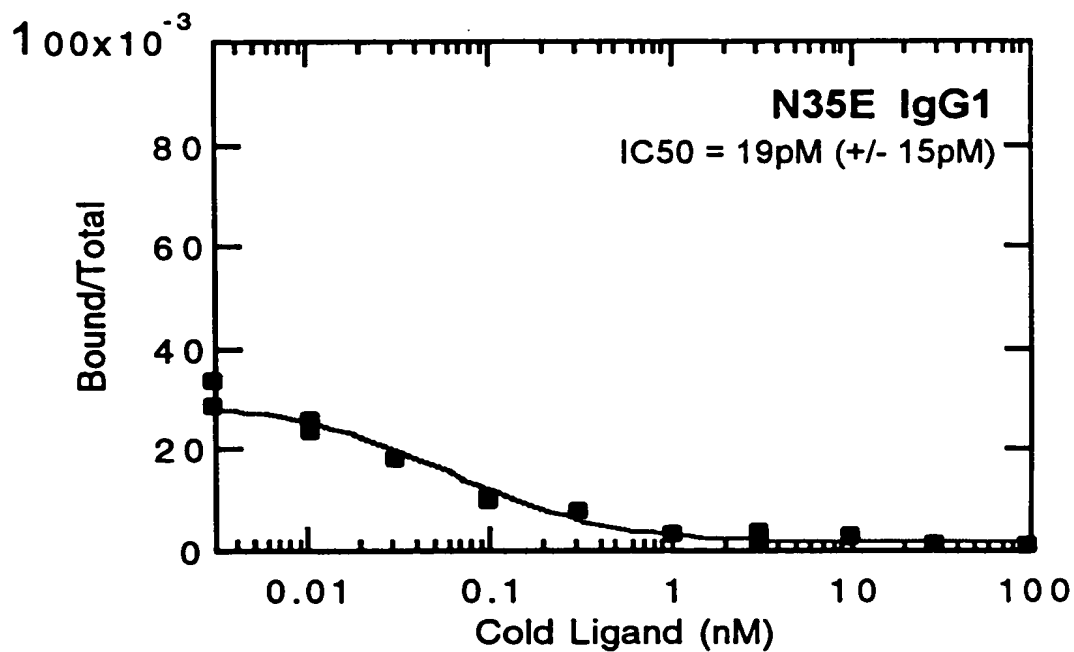


FIG. 52B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
TTTTCCCATATA GATCTCCAAC TCCACTAAAA TACTTTTTTCT TATAGCGTAA AGAAGAACGT
-1 M K K N I A F L L A

841 TCTATGTTTCG TTTTTTCTAT TGCTACAAAC GCGTACGCTG AGGTTCAGCT AGTGCAGTCT
AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
-11 S M F V F S I A T N A Y A E V Q L V Q S

901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACTATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTCCC GGACCTTACC
28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCTGATGG ACGTCTACTT GTCGGACGCA
68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCCTAA TAGCGATGTT ACCACTGACC
88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
AAGAAGCTGC AGACCCAGT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCC
108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC
128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
CCGACGGACC AGTTCCTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCCCGGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
GACTGGTCGC CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG
168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
TCGTGCGACC ACTGGCACGG GAGGTGCTCG AACCCGTGGG TCTGGATGTA GACGTTGCAC
188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
TTAGTGTTTCG GGTGCTGTGT GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCCCGCCGTGA (SEQ ID NO.69)
TGAGTGTGTA CGGGCGGCACT
228 T H T C P P O (SEQ ID NO.70)

FIG. 53



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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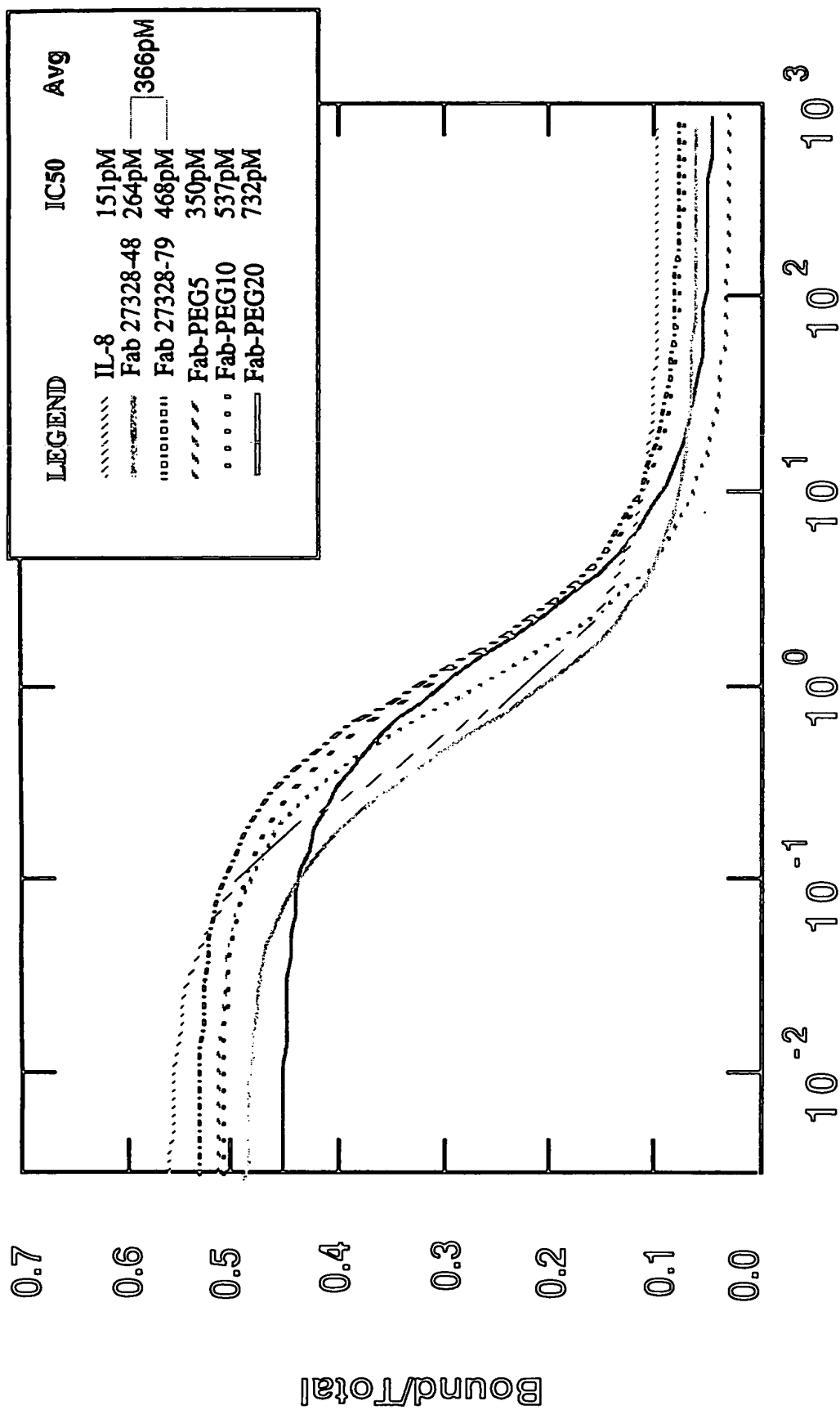


FIG. 54A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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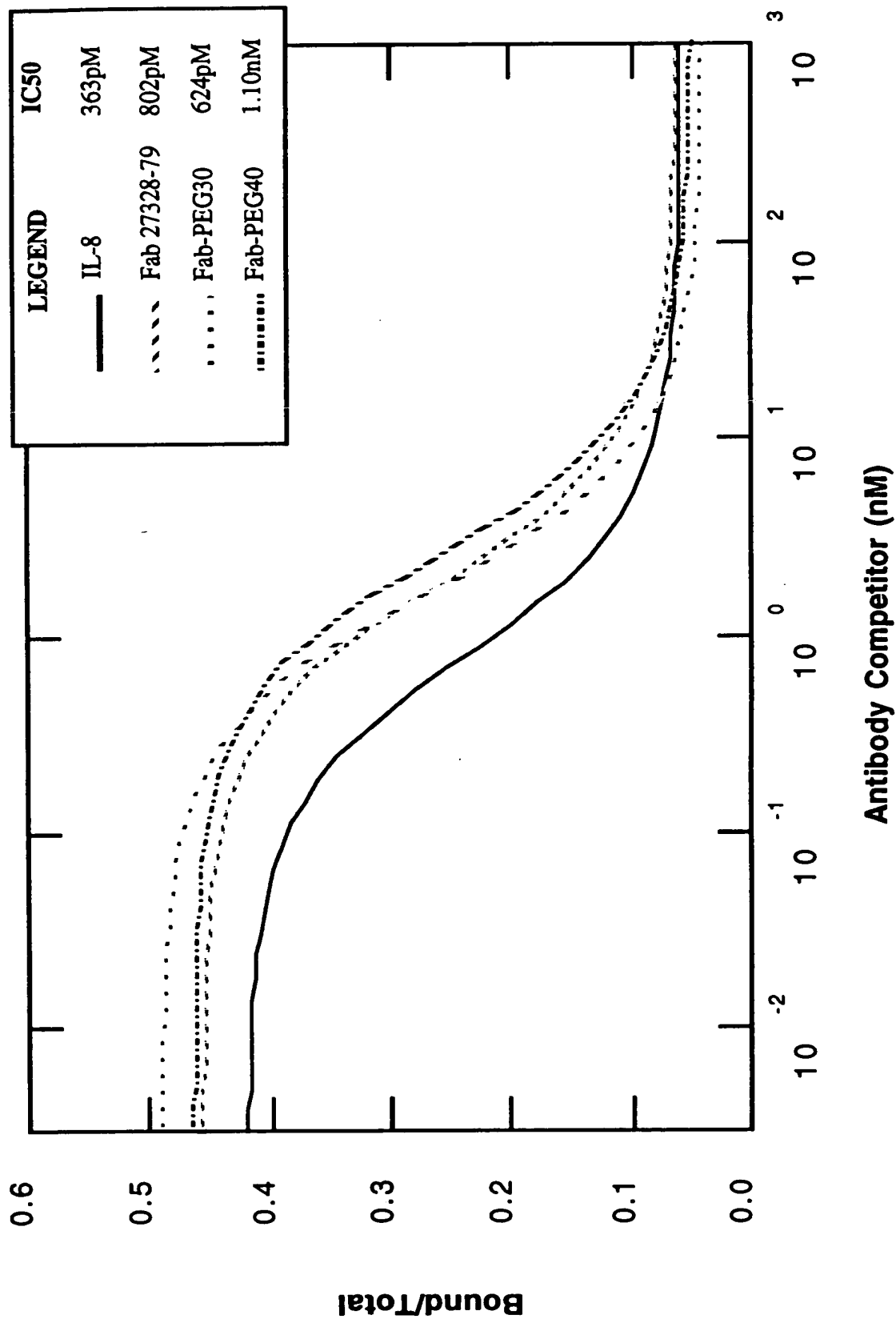


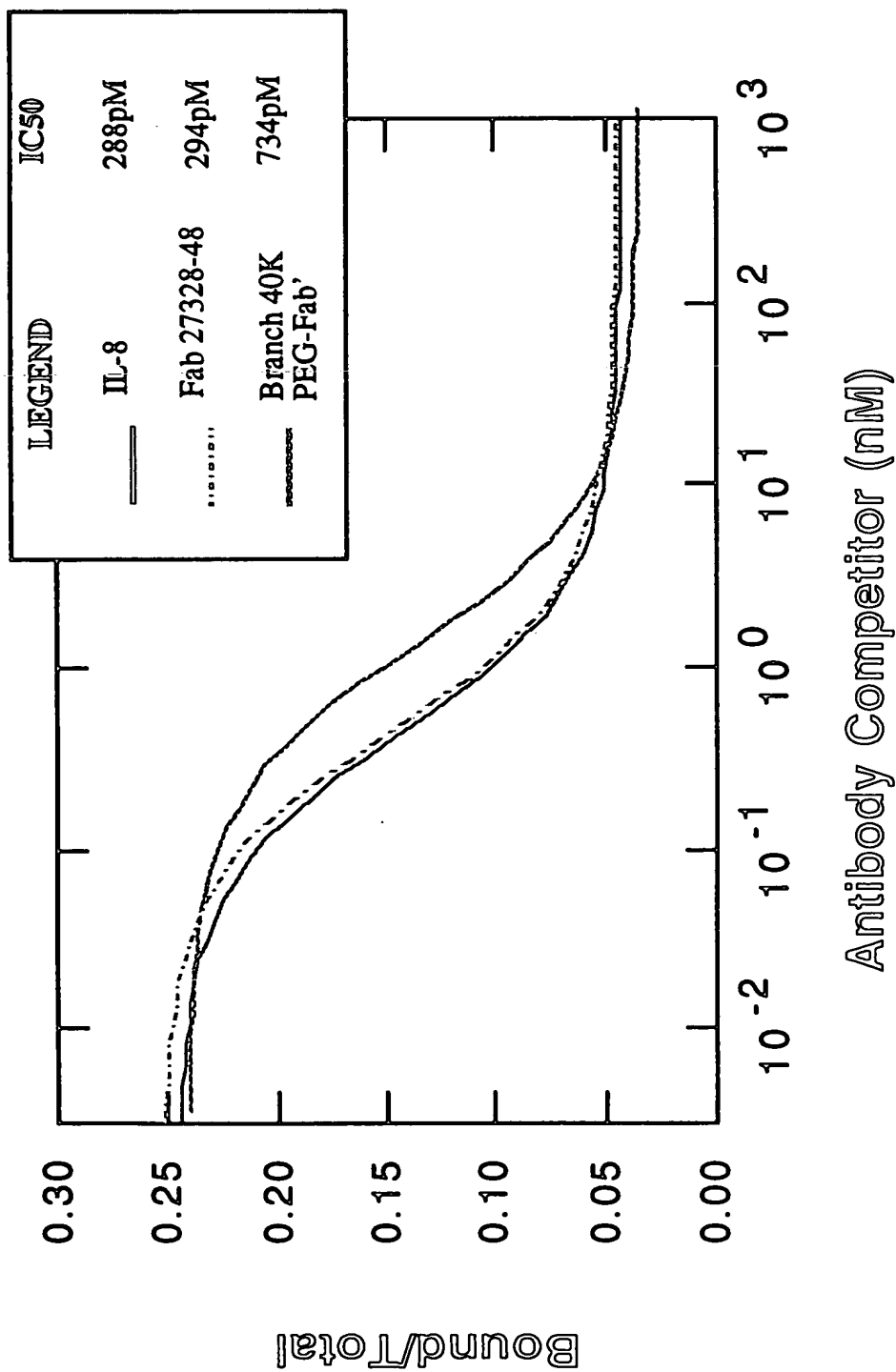
FIG. 54B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

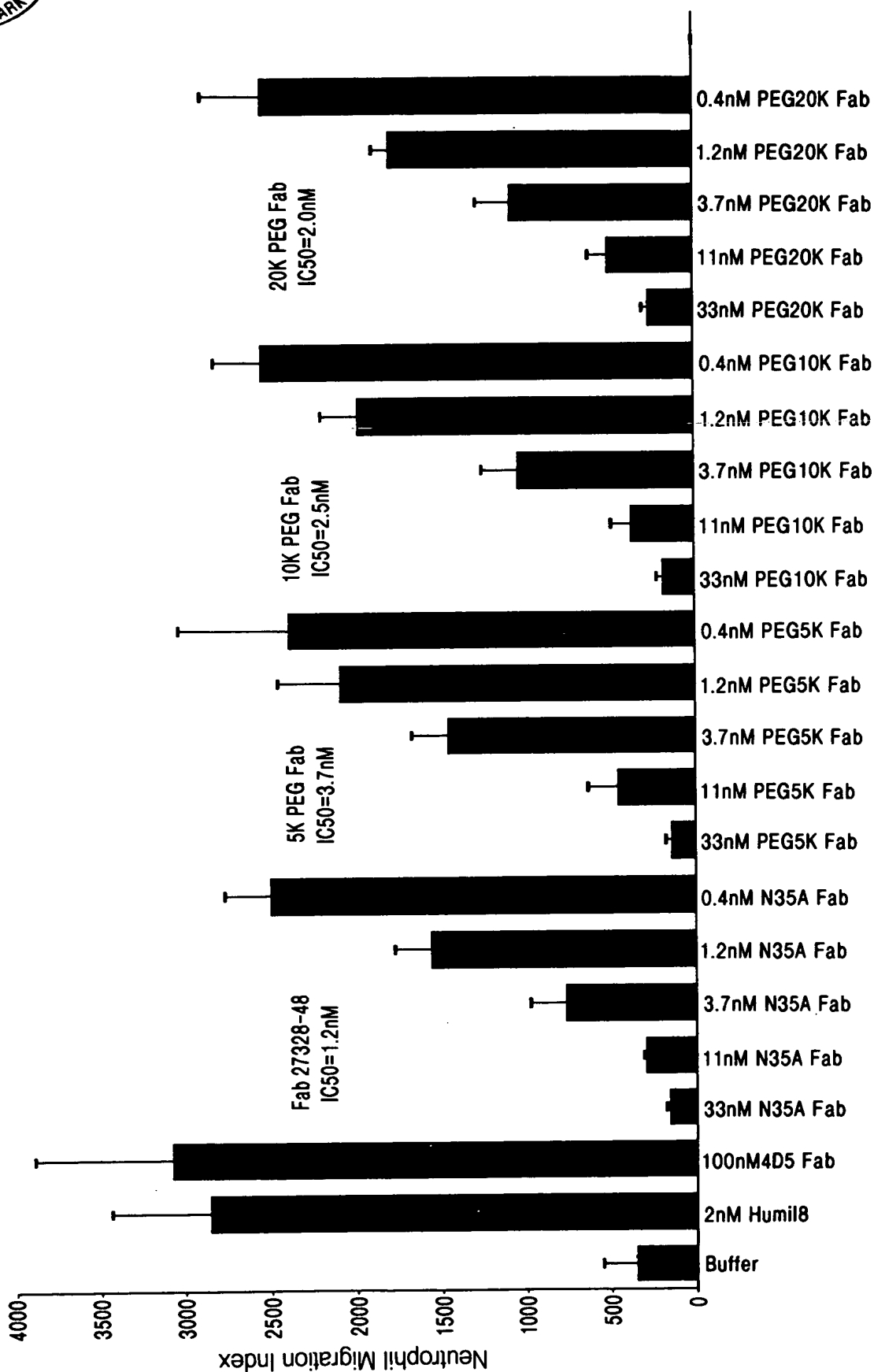


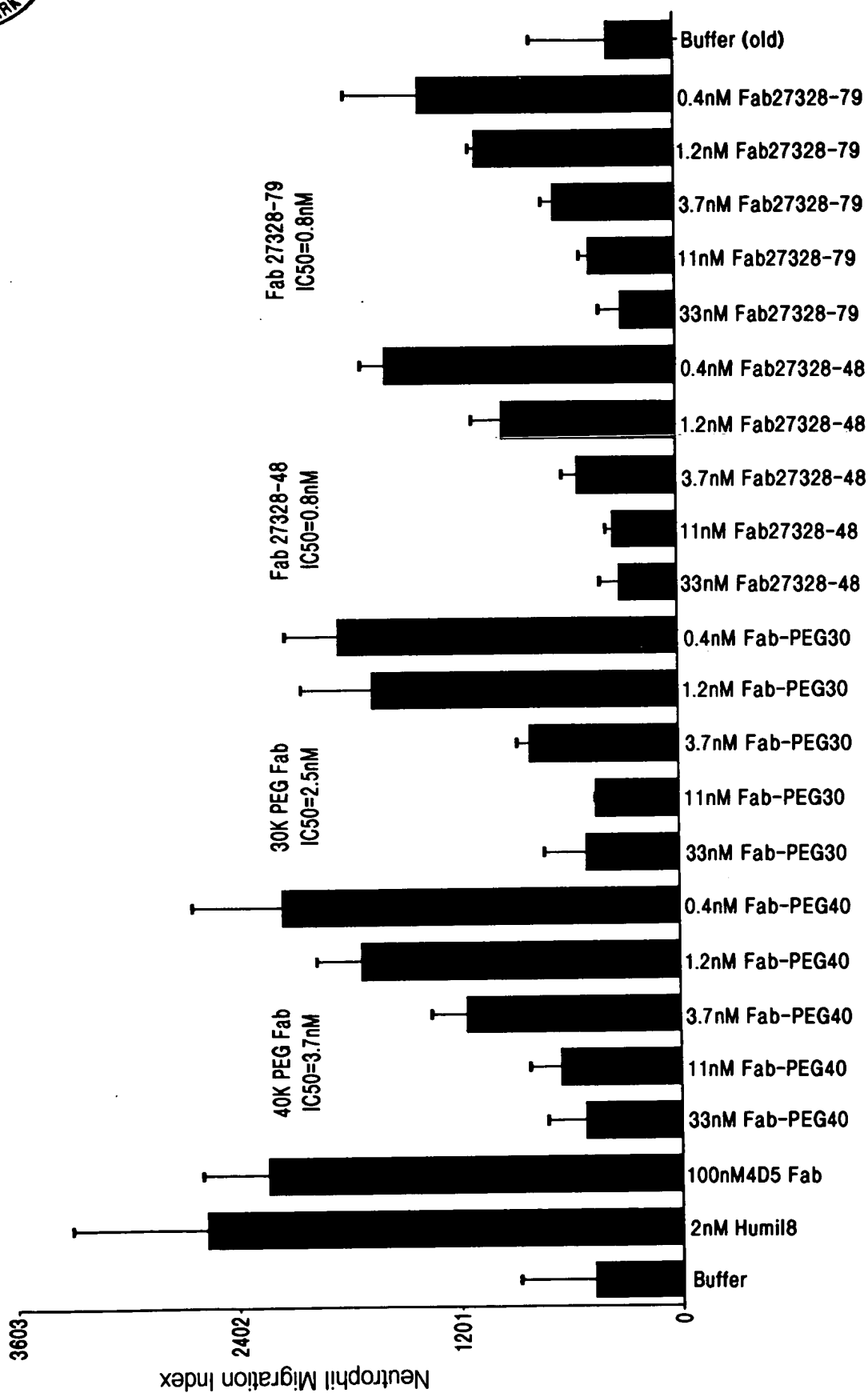
FIG. 55A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

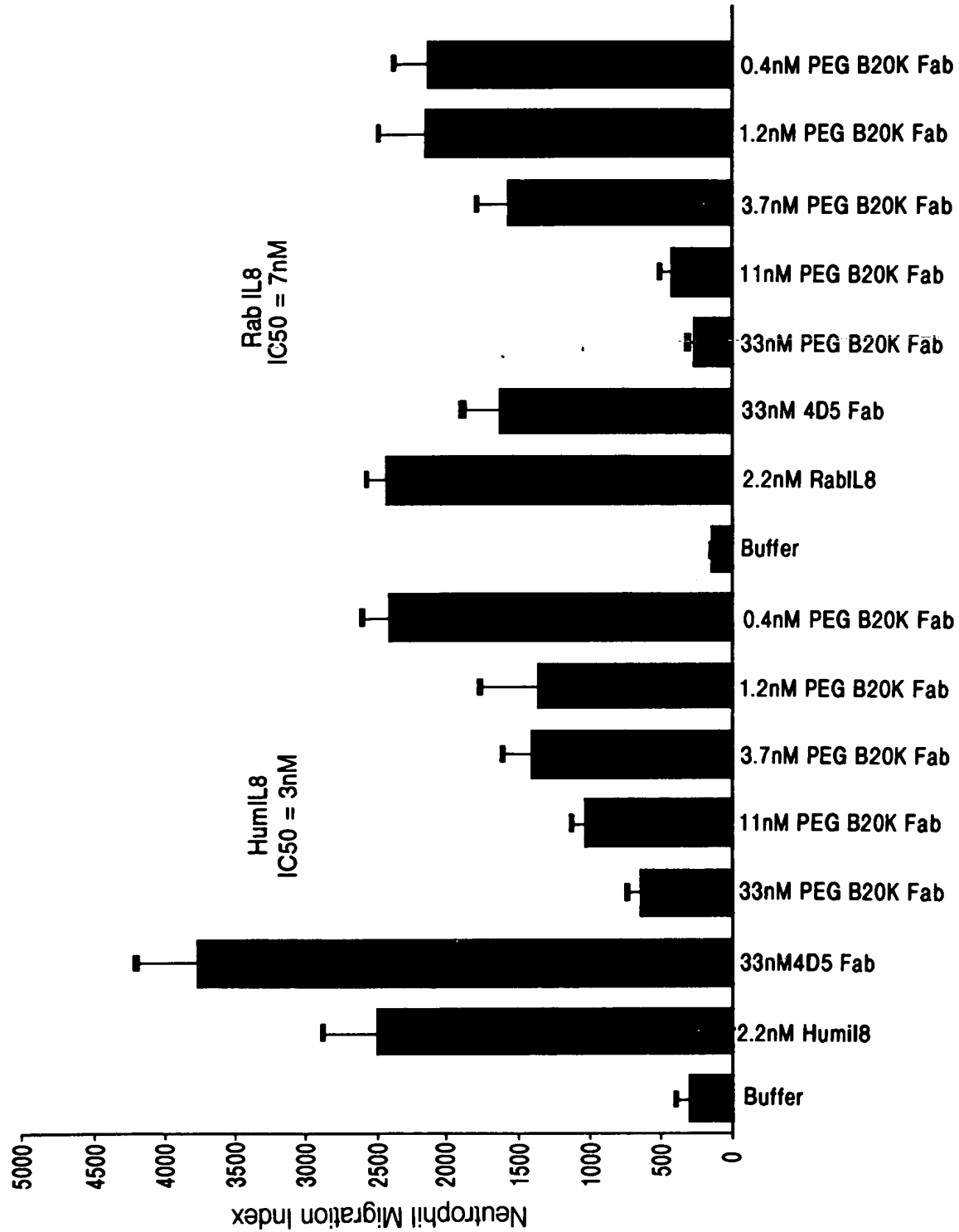


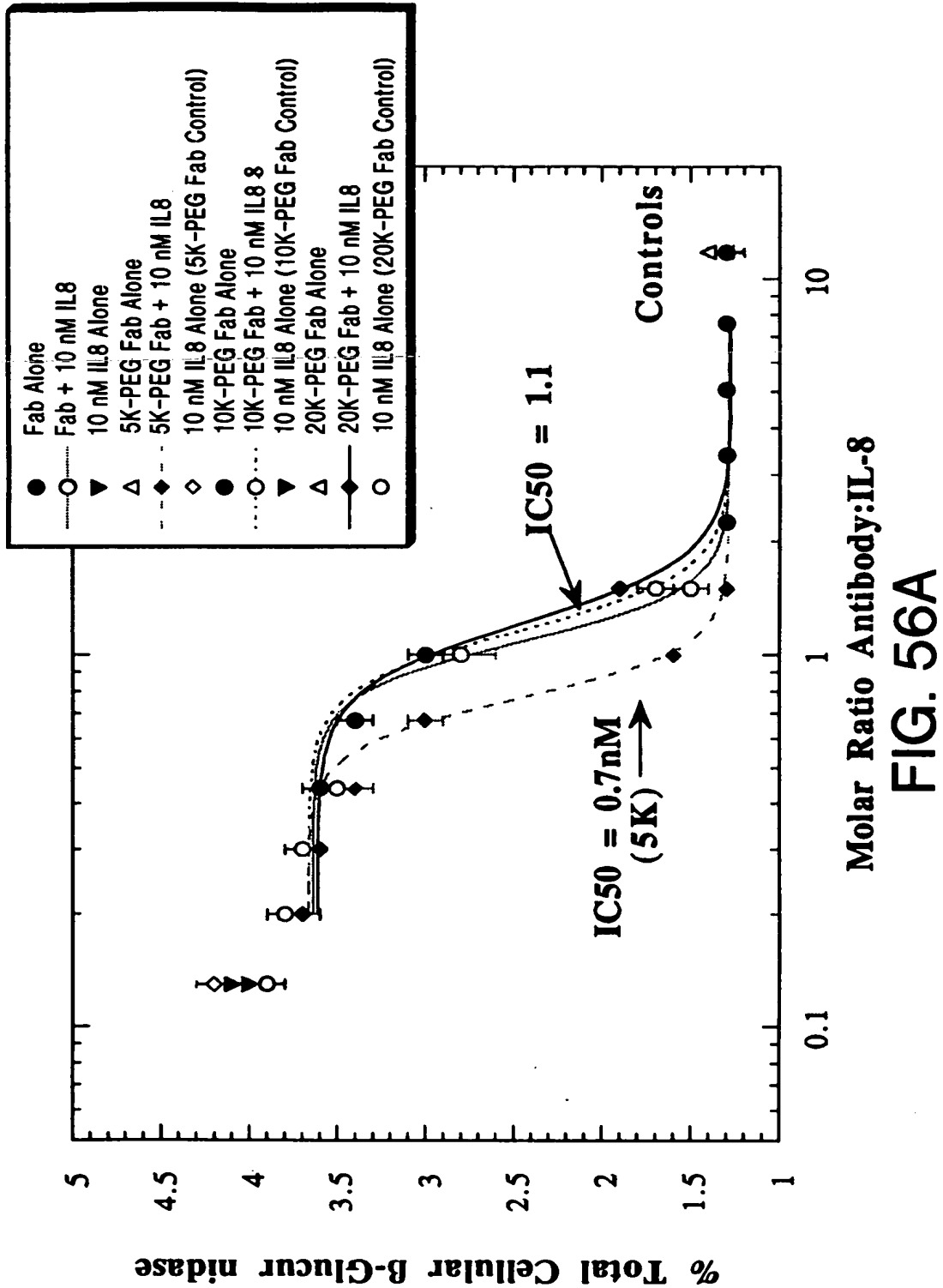
FIG. 55C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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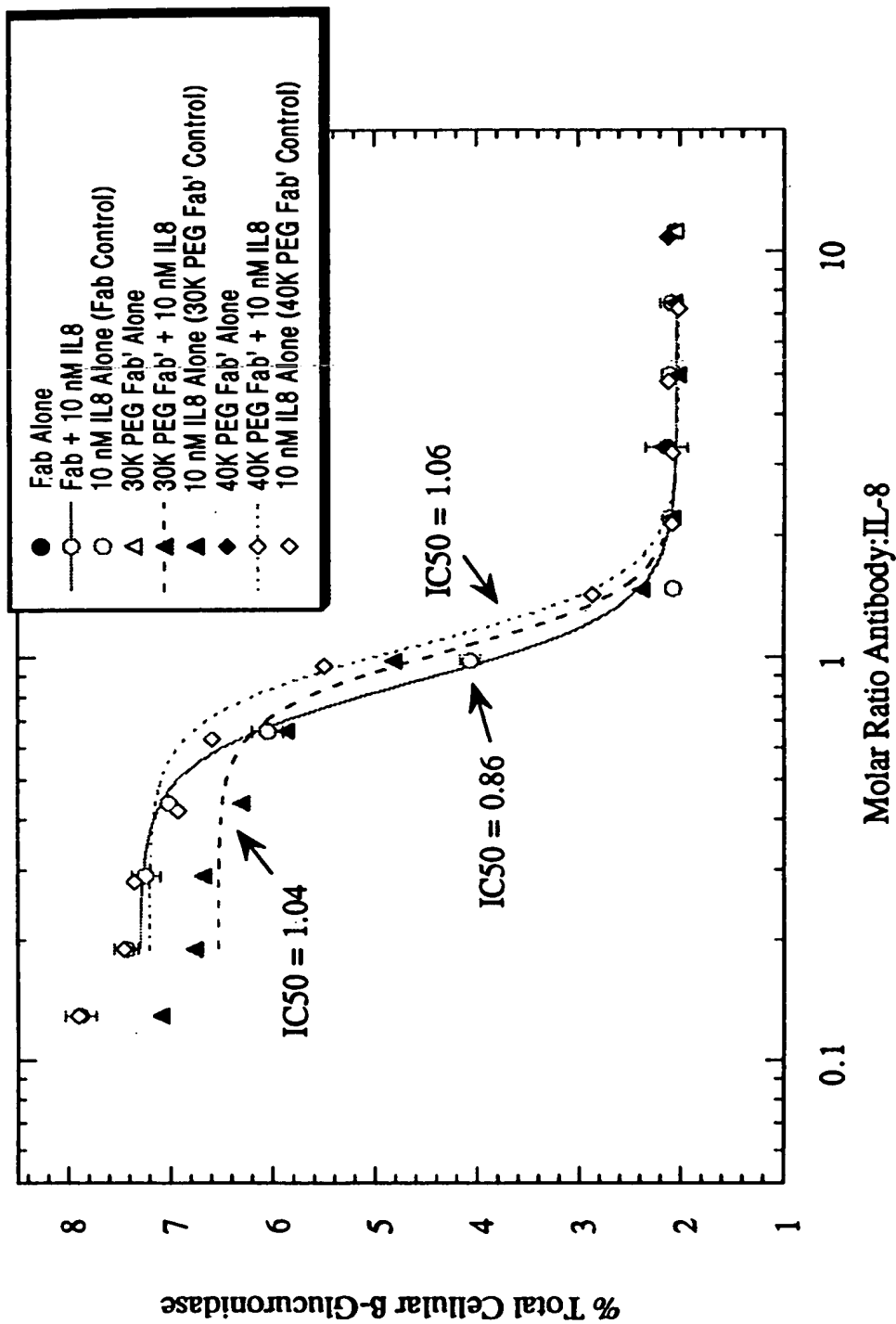


FIG. 56B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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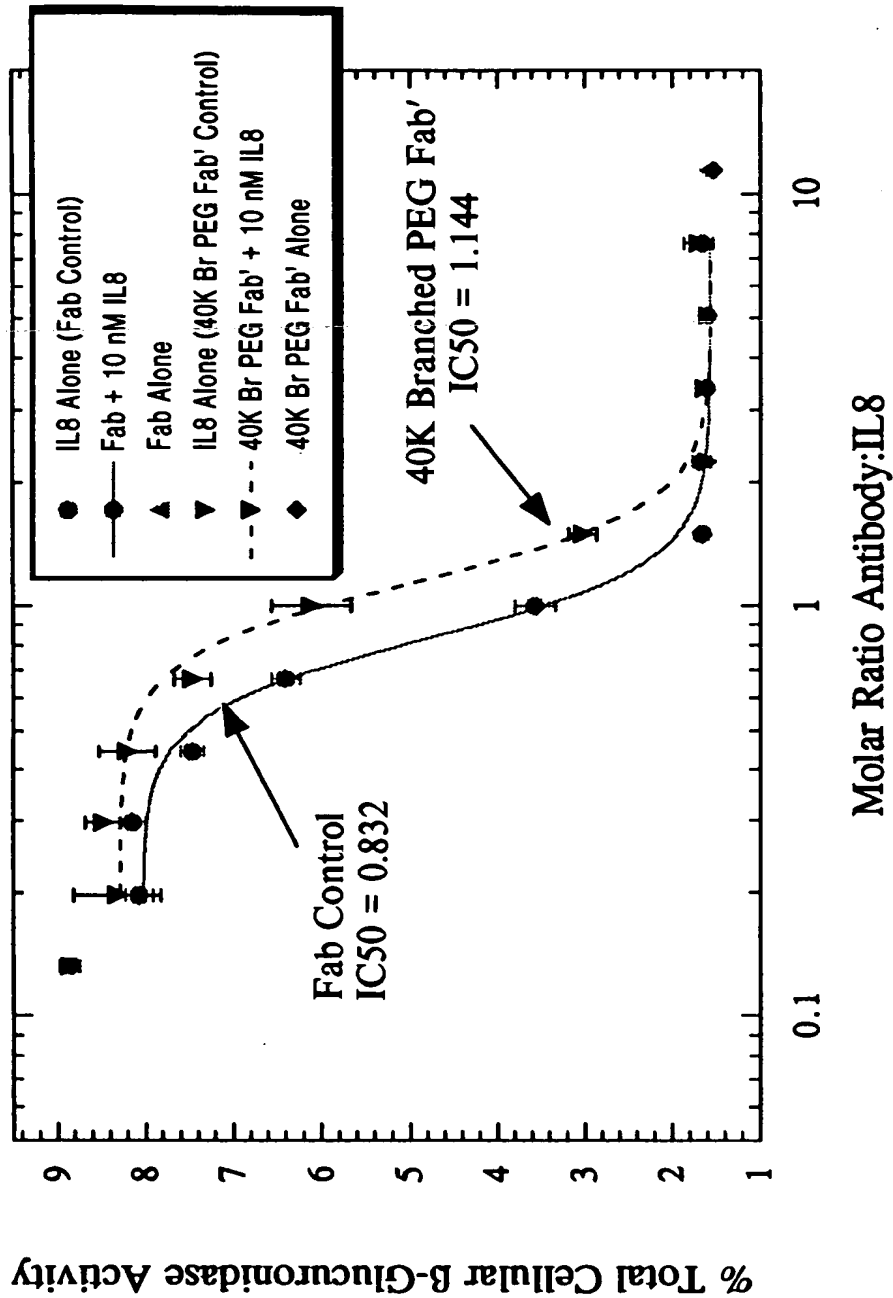


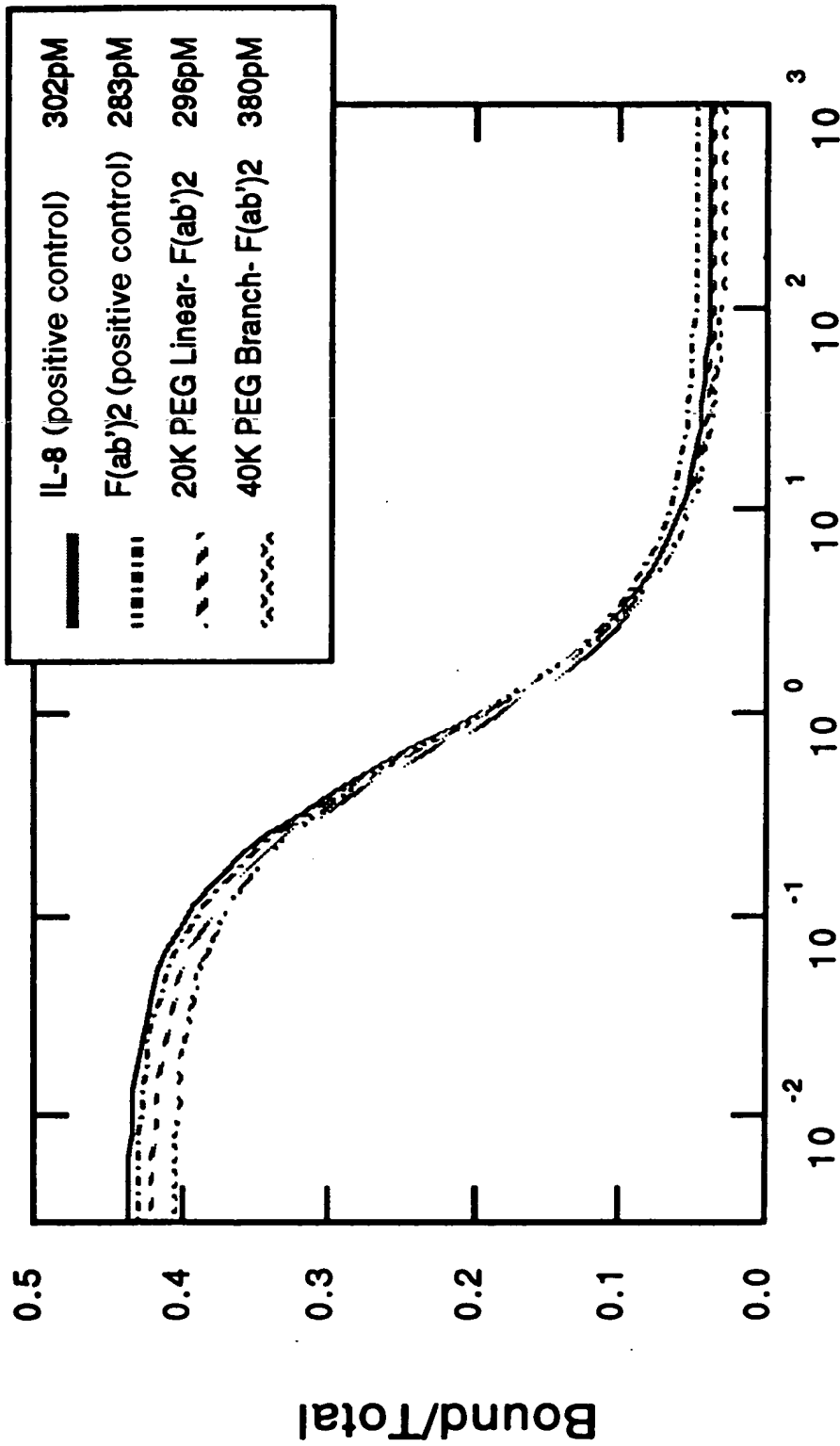
FIG. 56C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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Pegylated F(ab')₂ (nM)

FIG. 57A

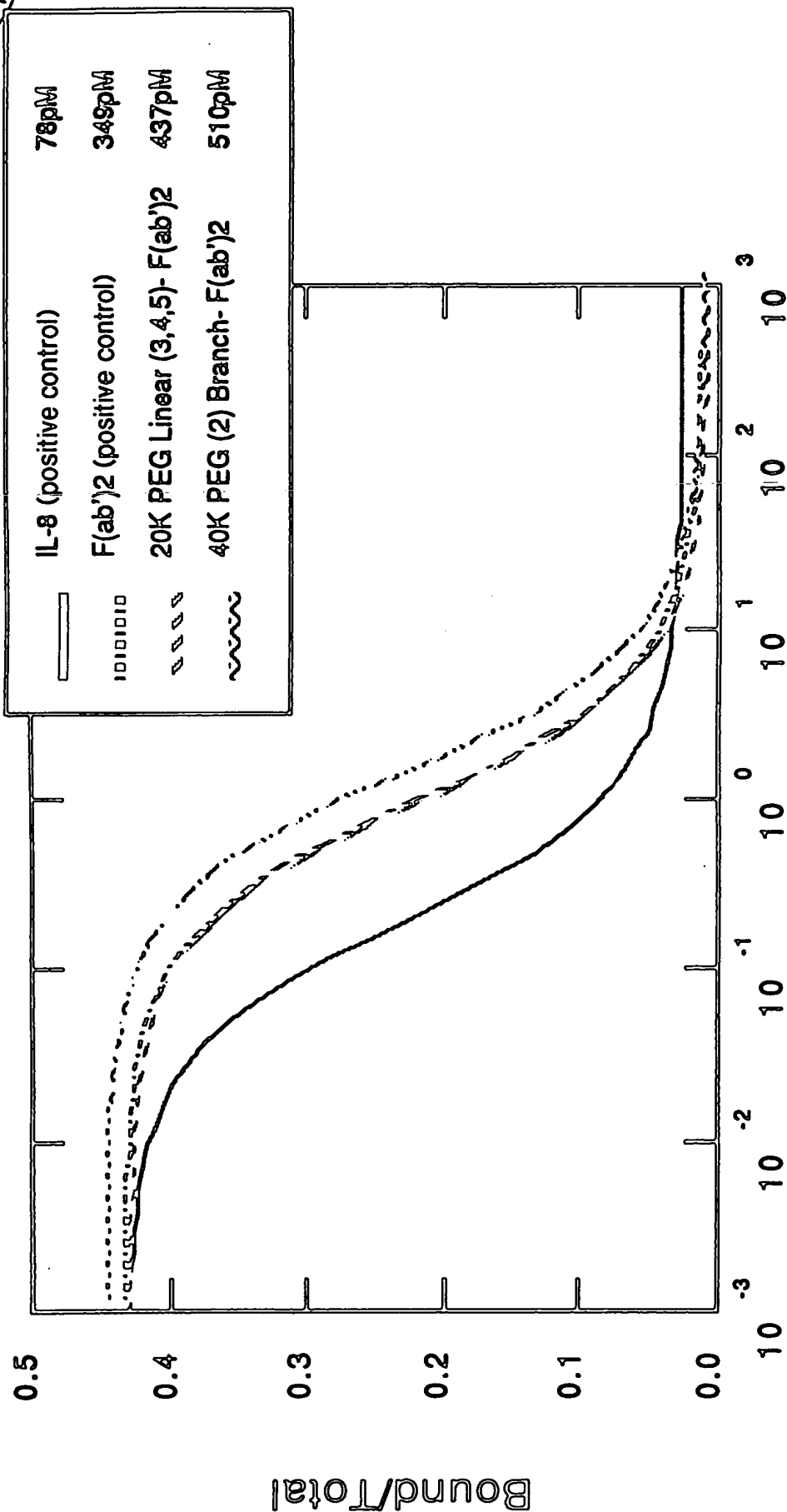


ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182

Atty Docket: GENENT.093A



Pegylated F(ab')₂ (nM)

FIG. 57B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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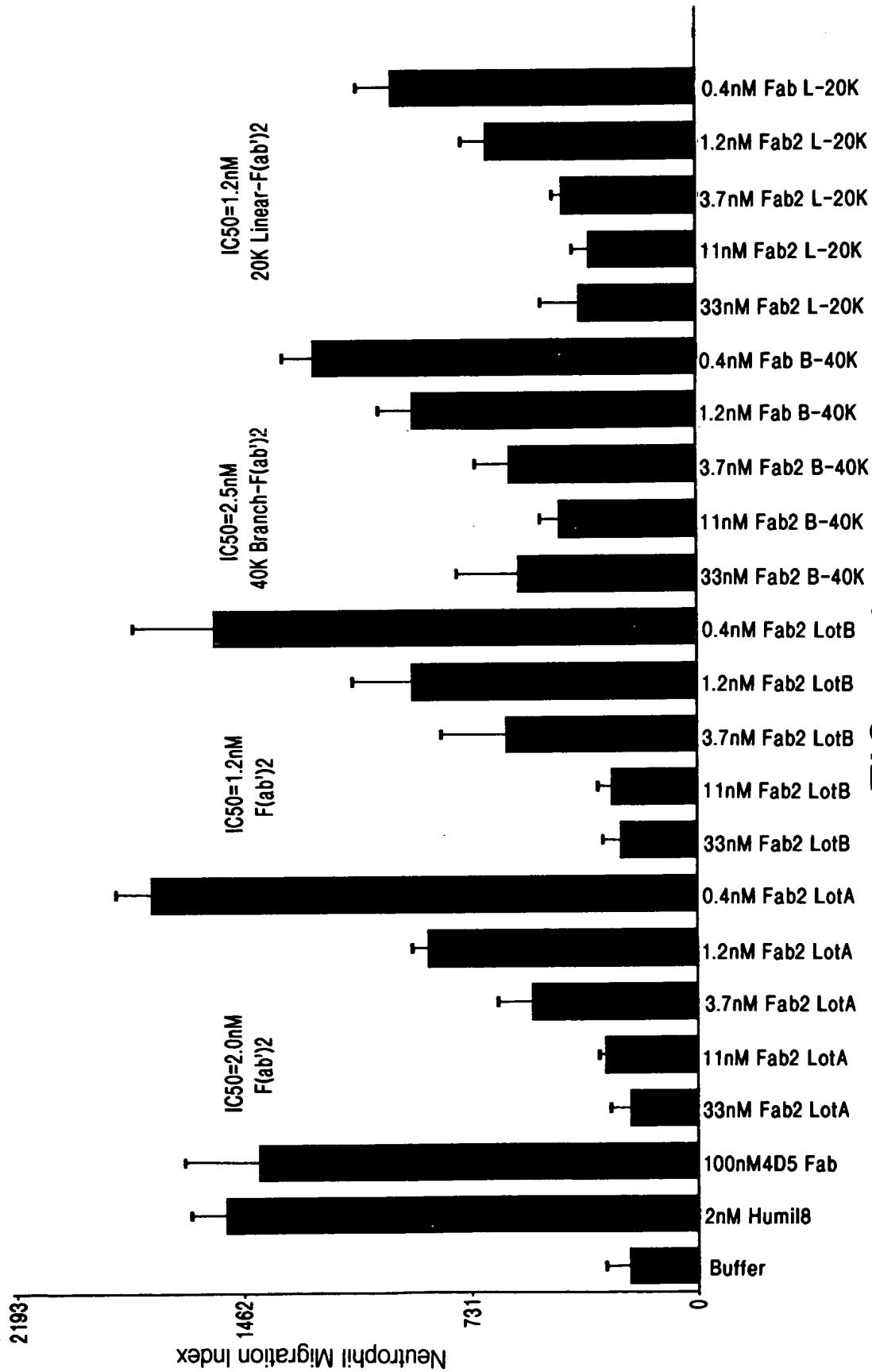


FIG. 58A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

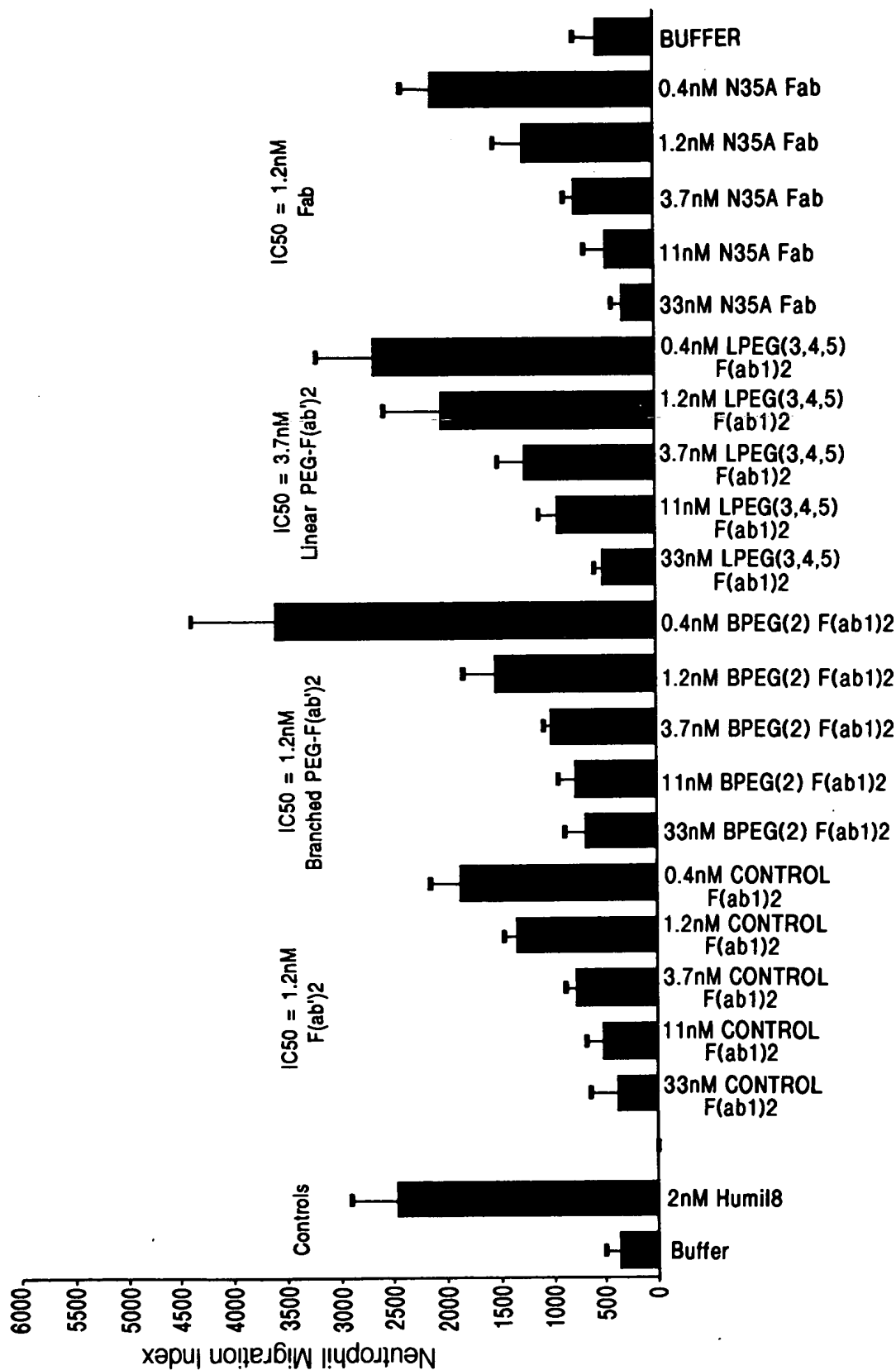


FIG. 58B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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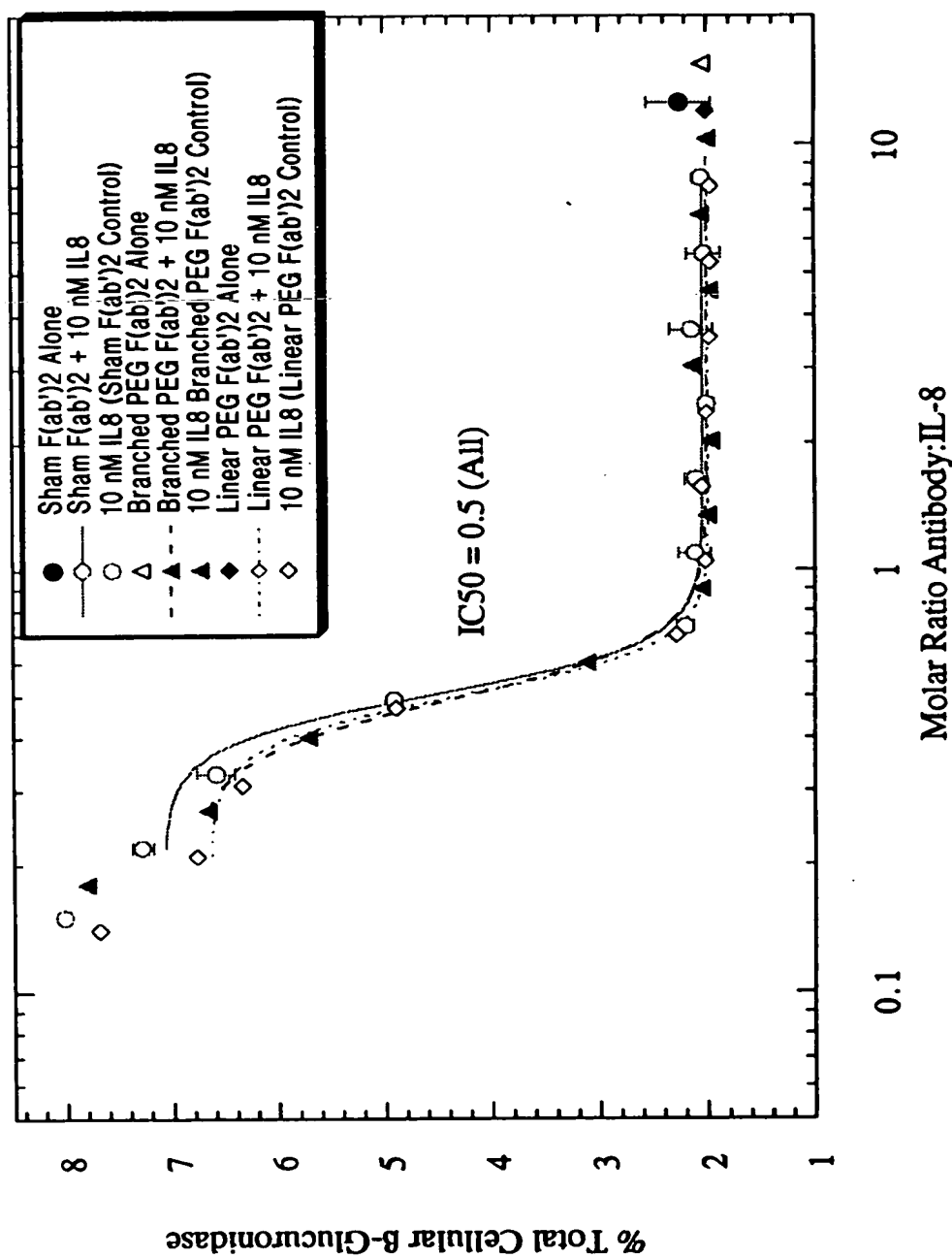


FIG. 59A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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Atty Docket: GENENT.093A

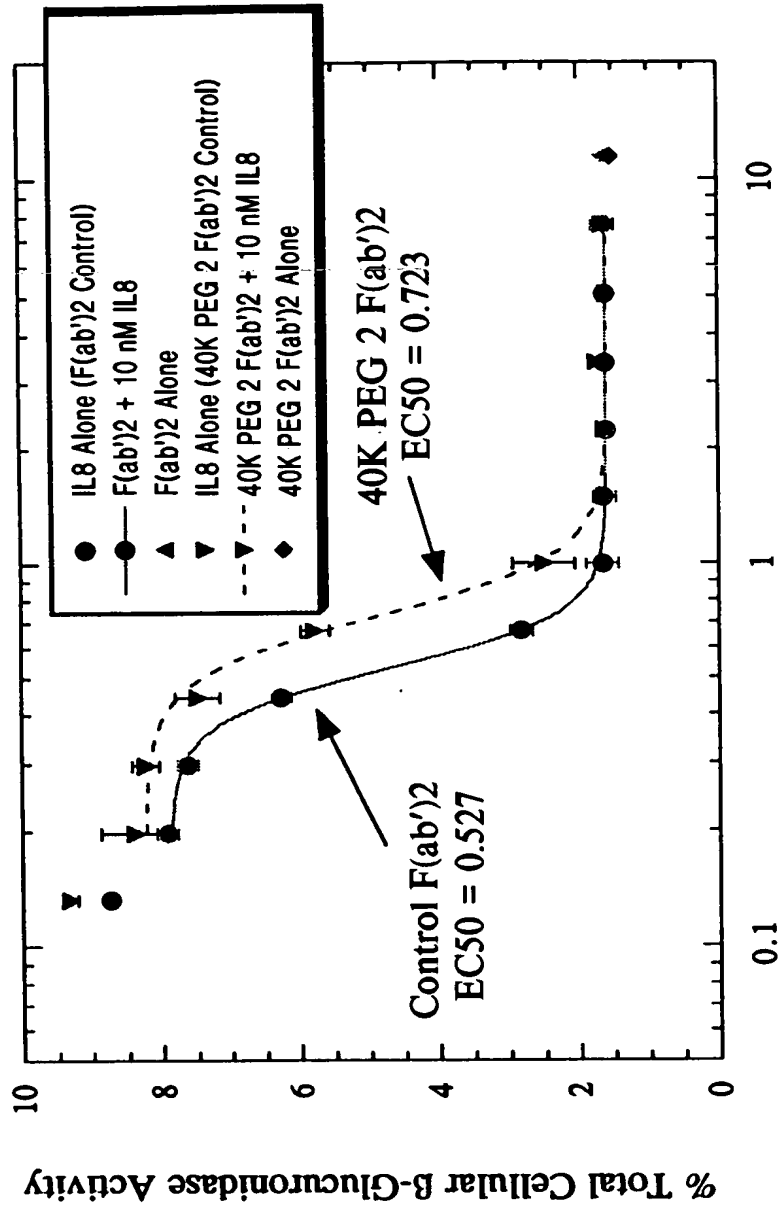


FIG. 59B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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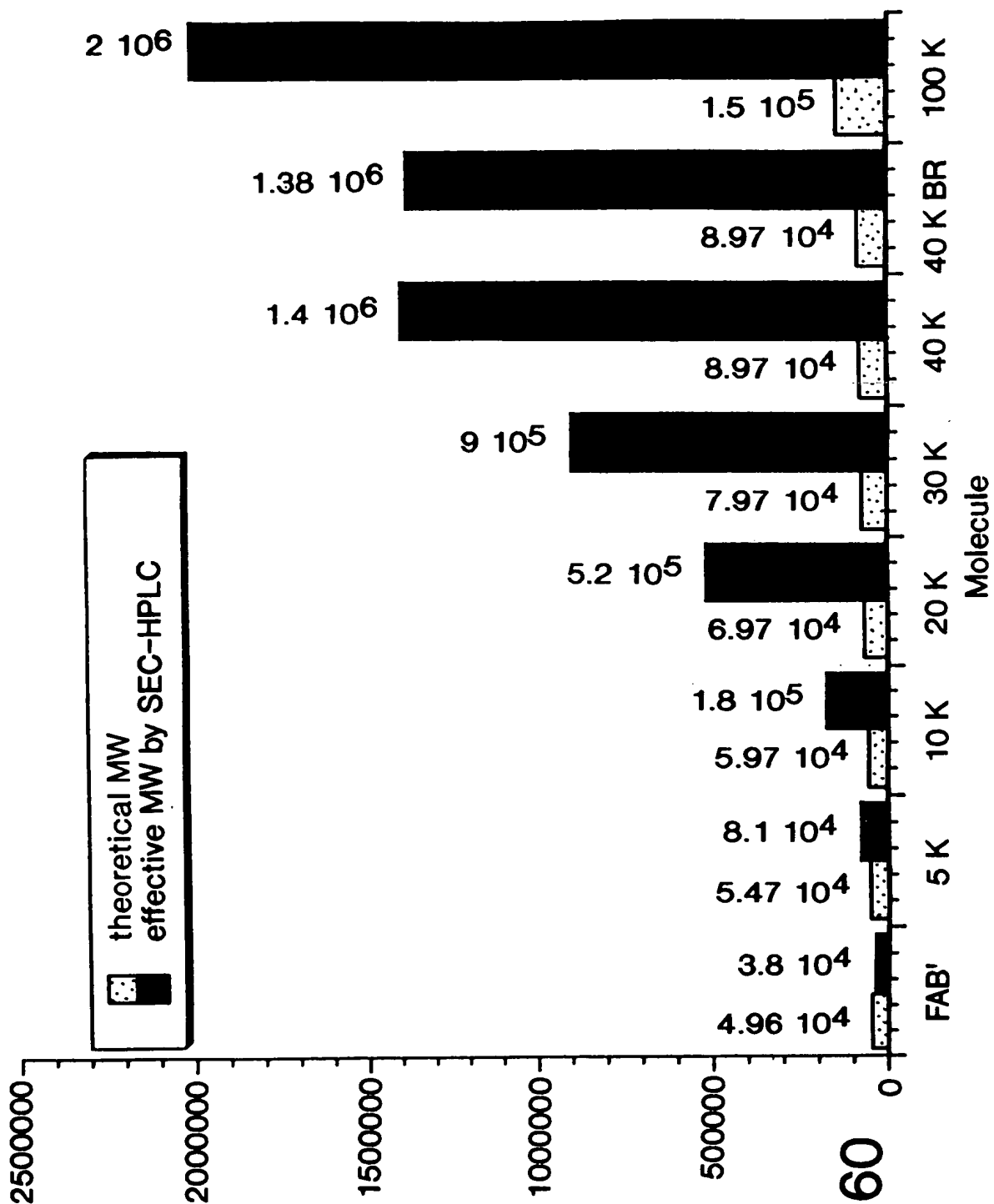
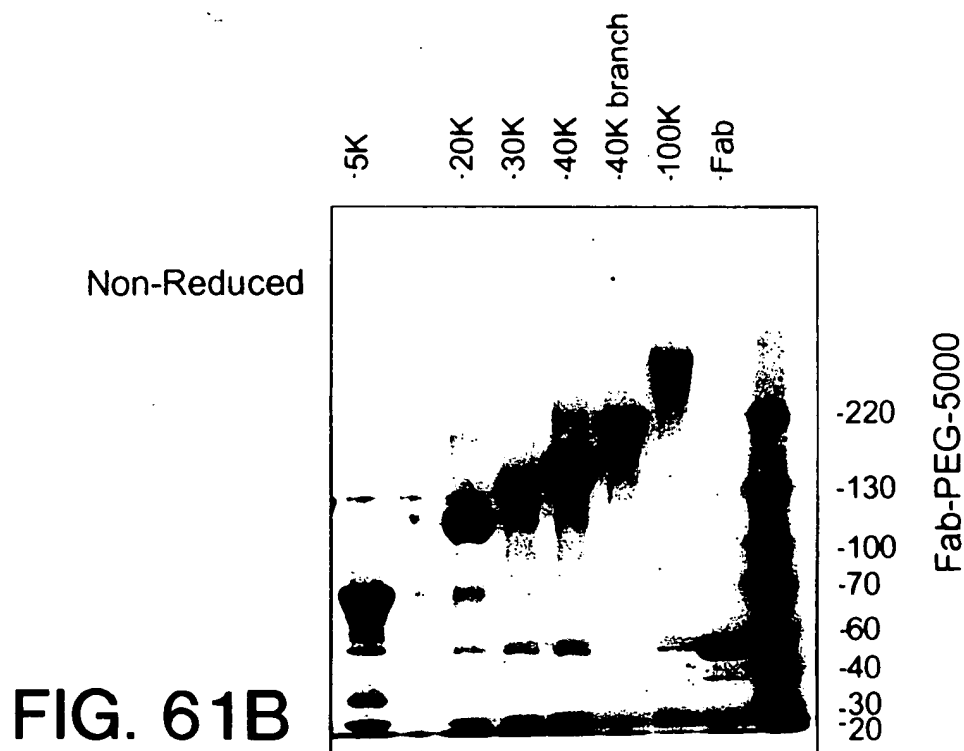
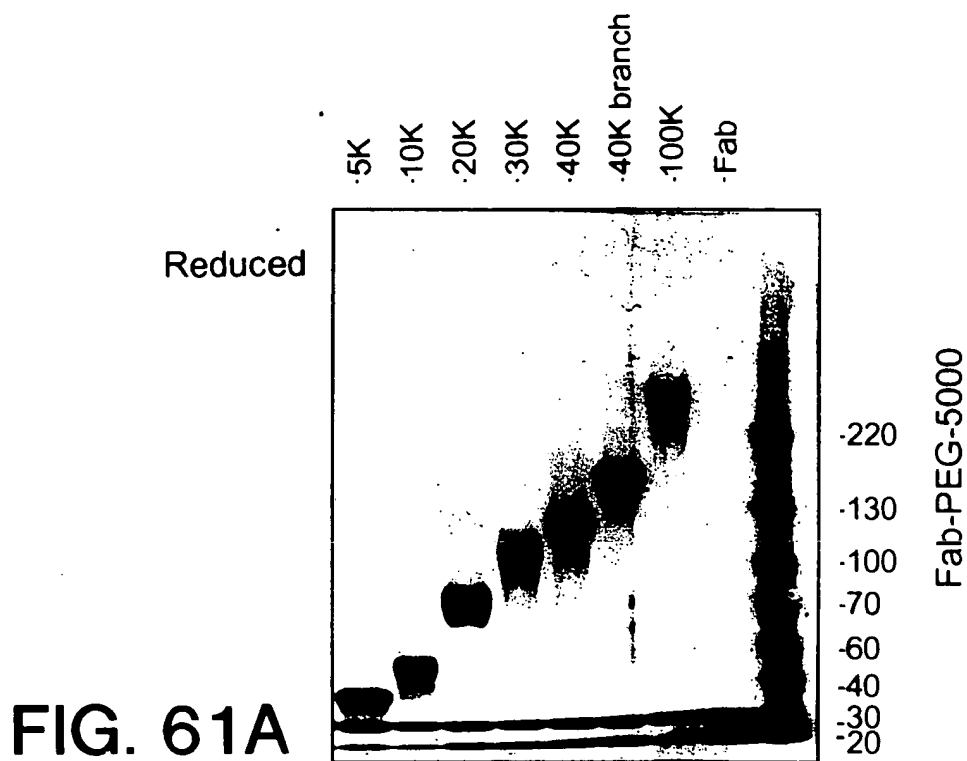


FIG. 60

MW (D)



10/21/02





ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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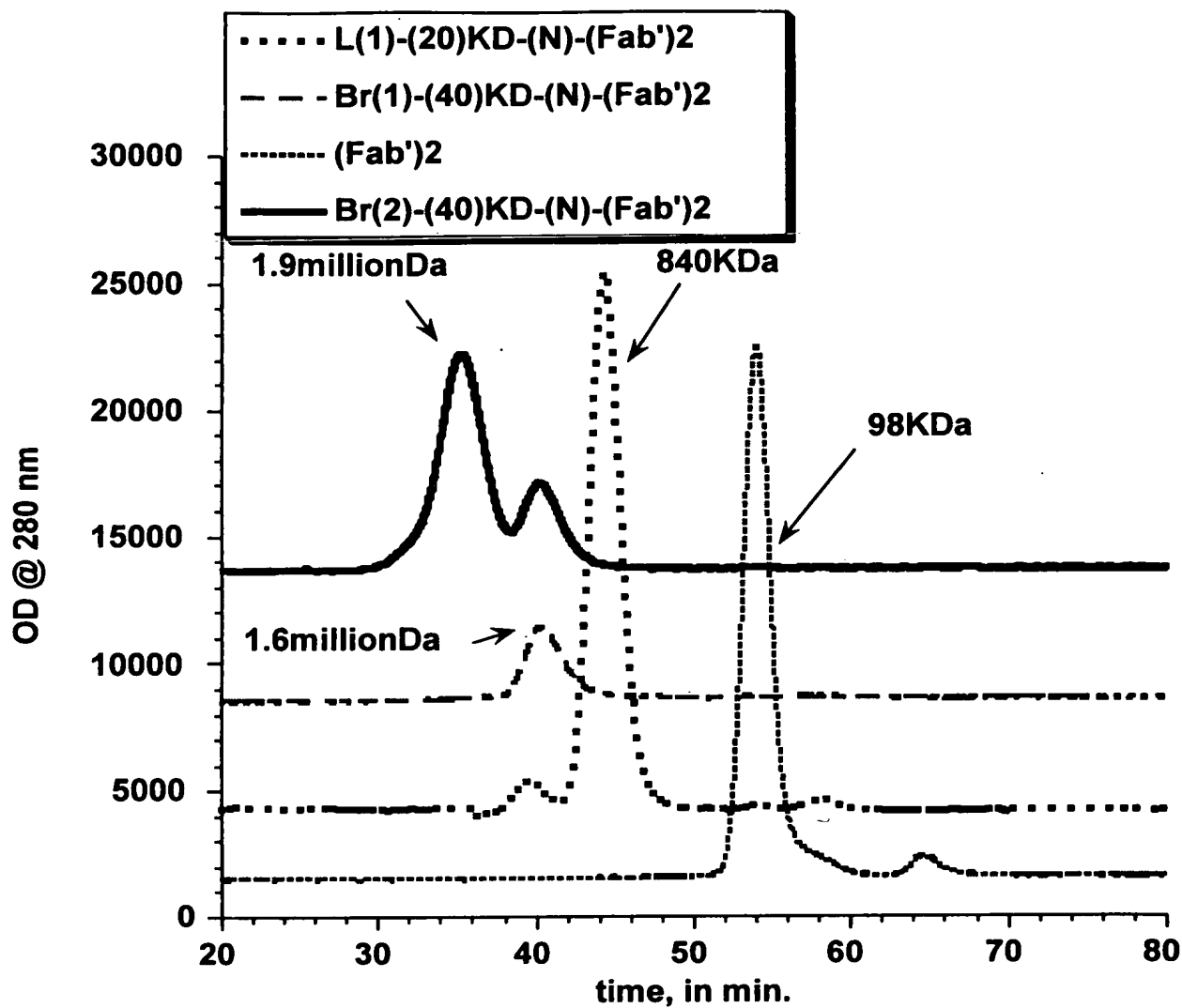


FIG. 62



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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Appl. No.: 09/234,182 Atty Docket: GENENT.093A

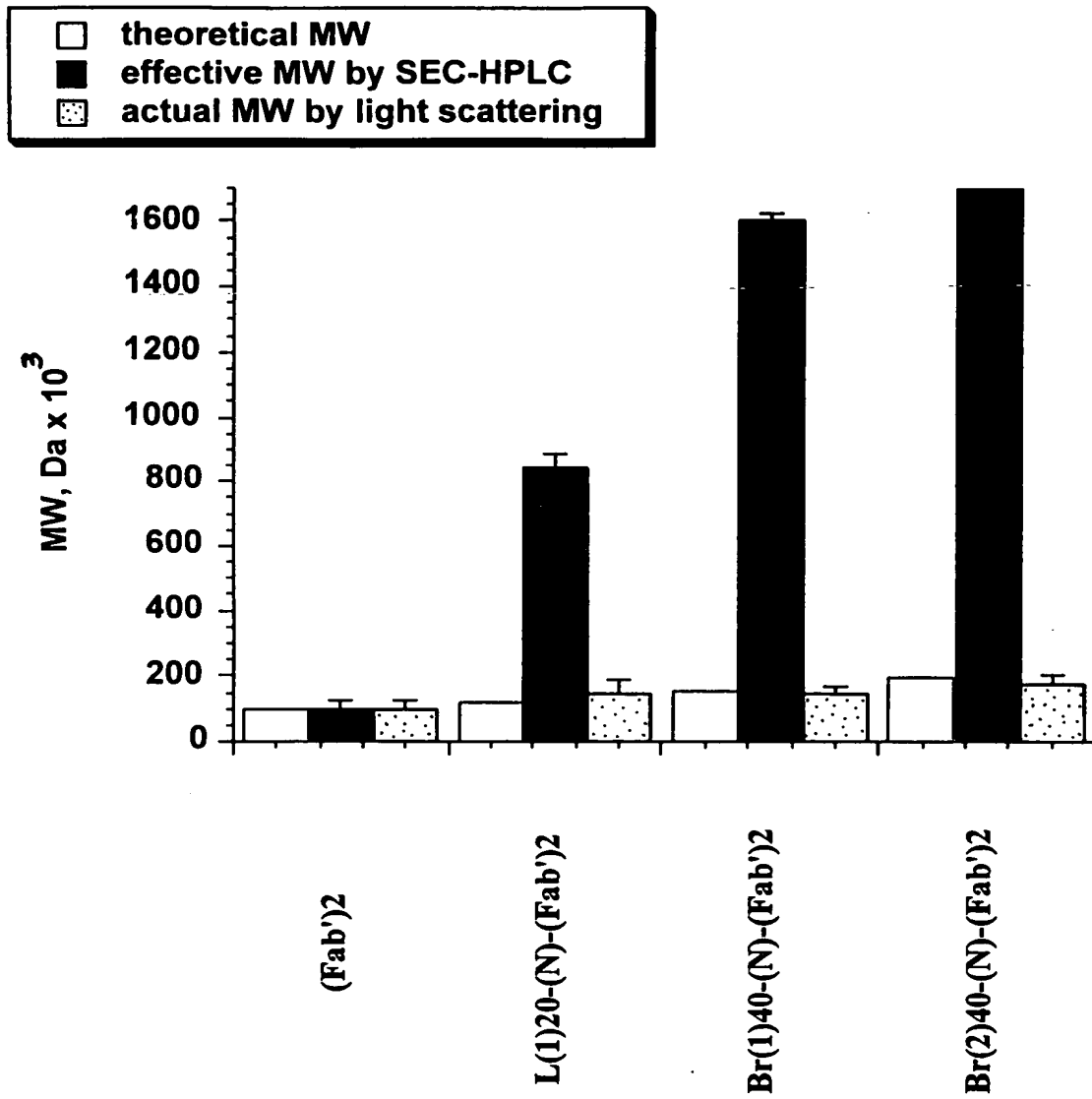


FIG. 63



10/21/02

ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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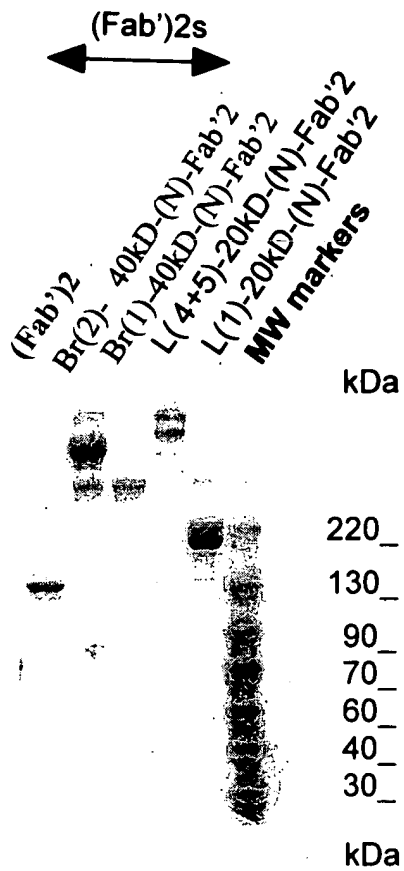


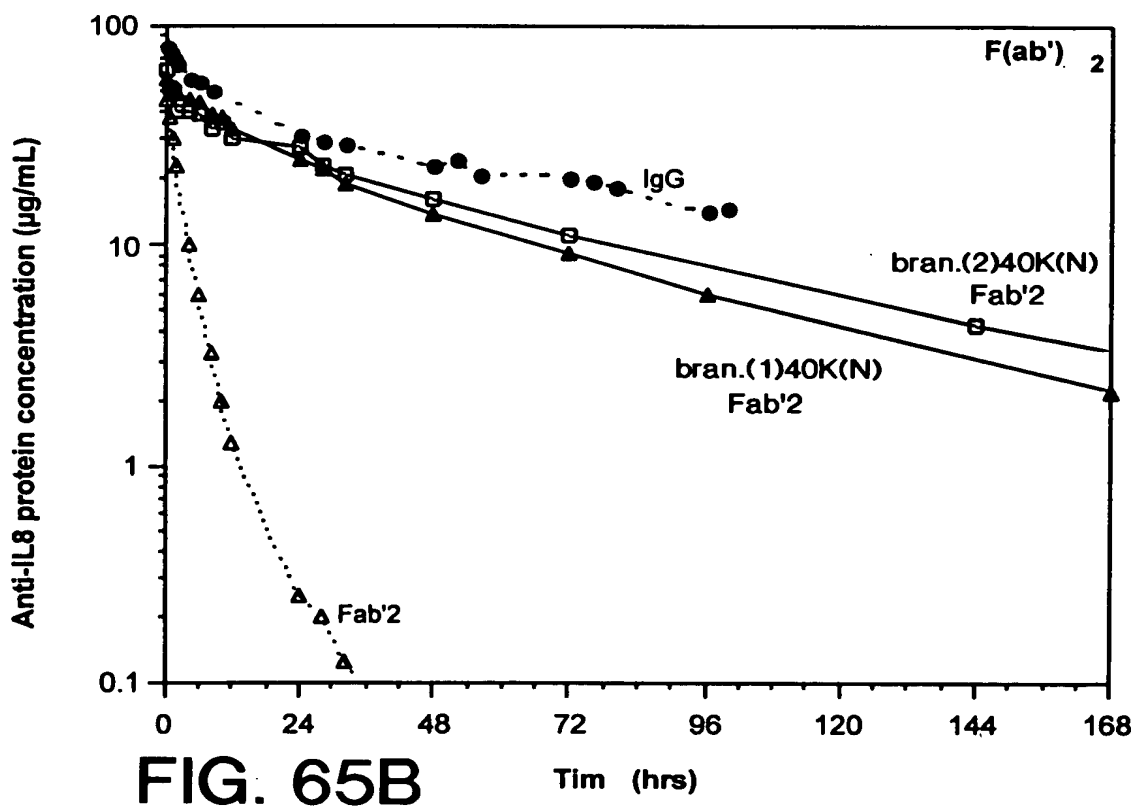
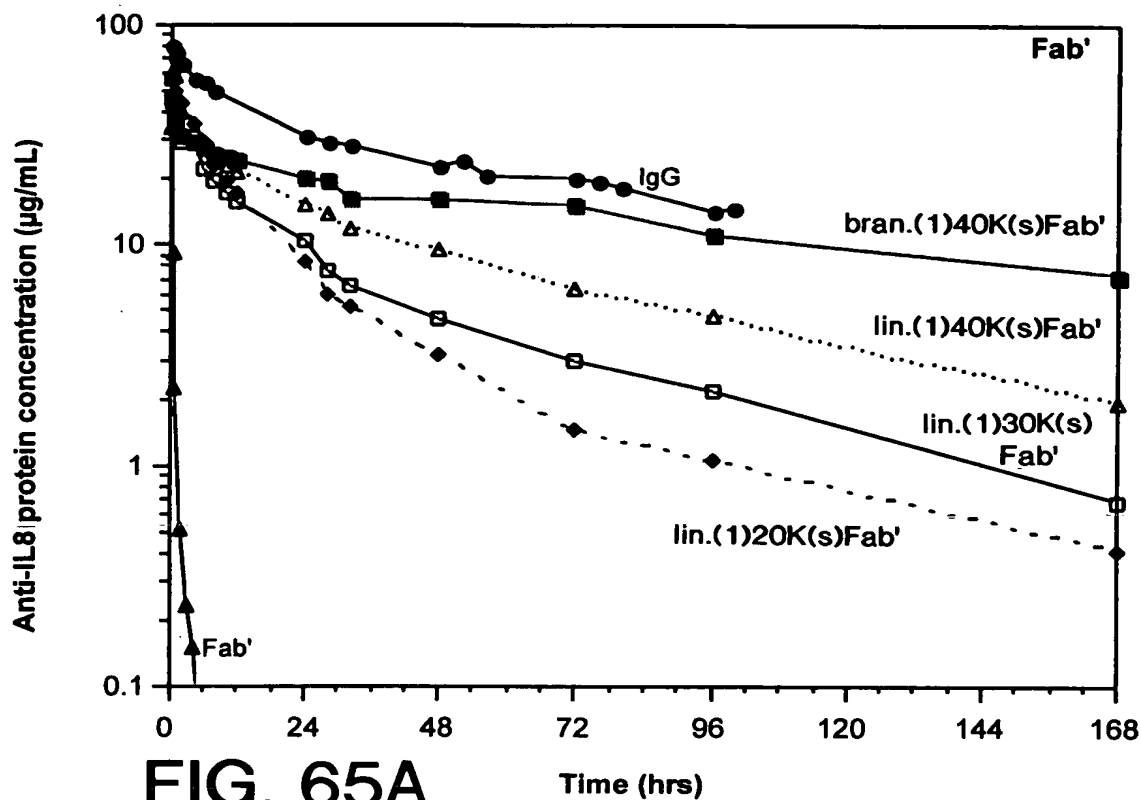
FIG. 64



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

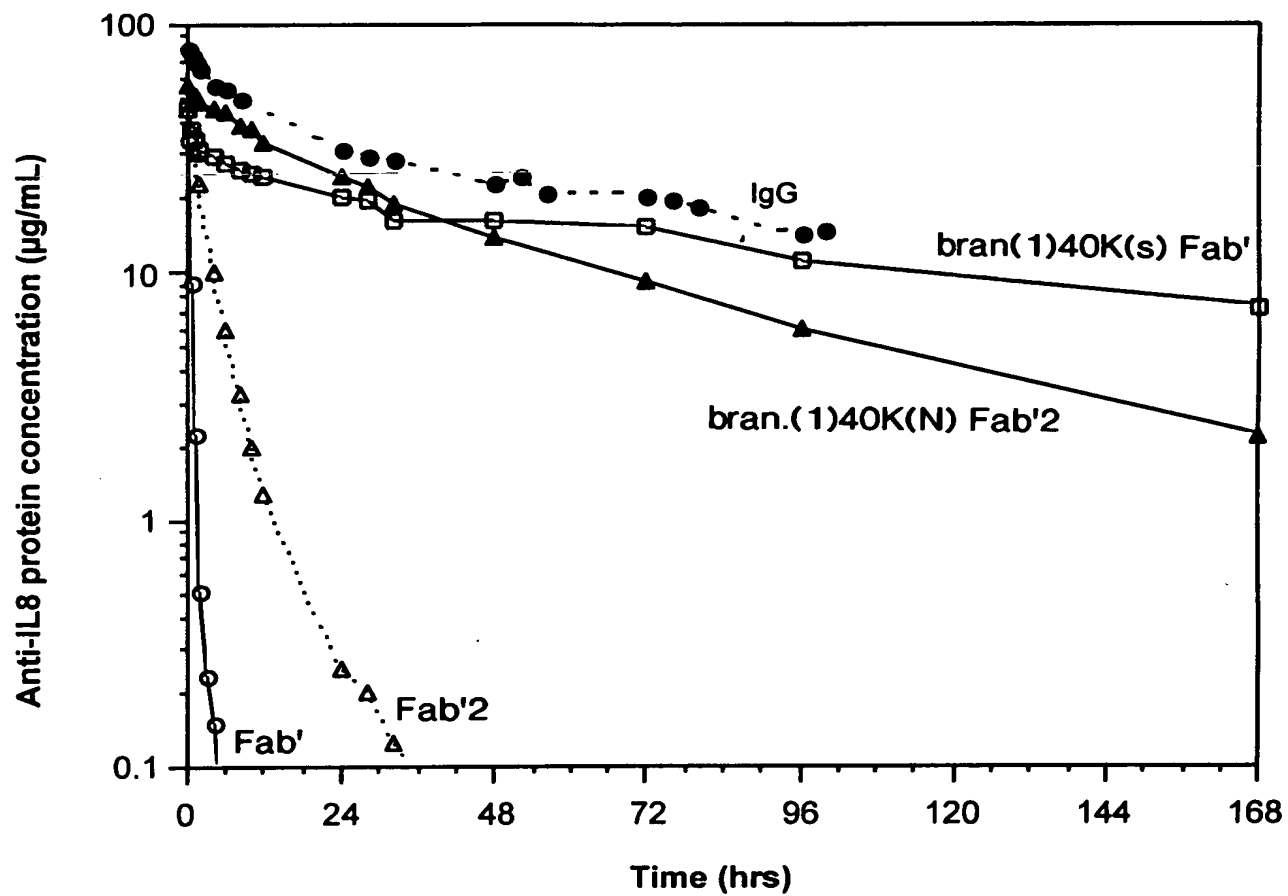


FIG. 66



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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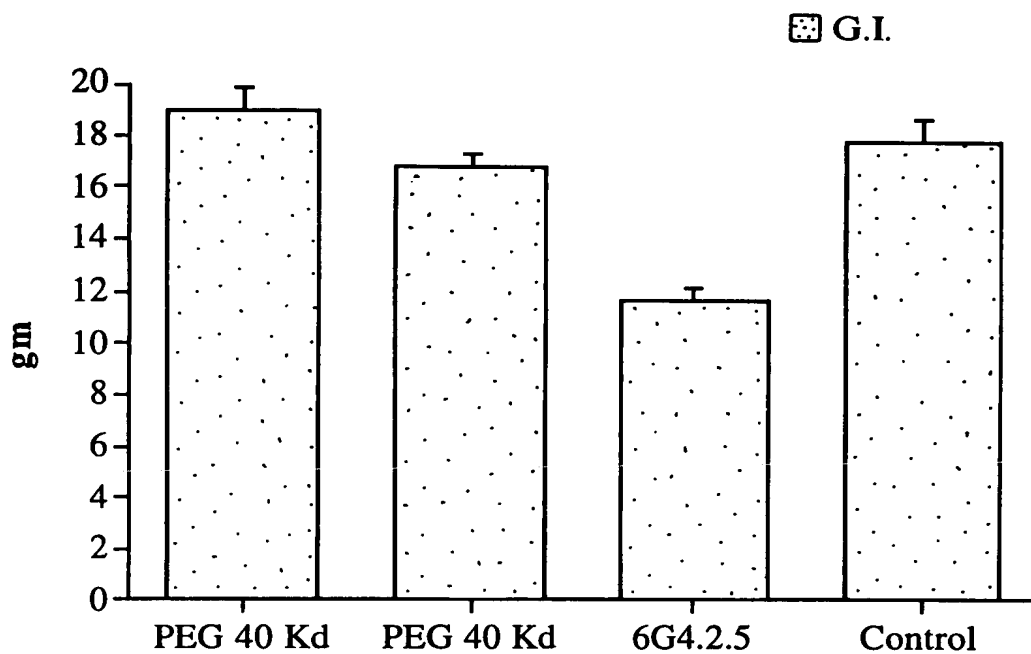


FIG. 67

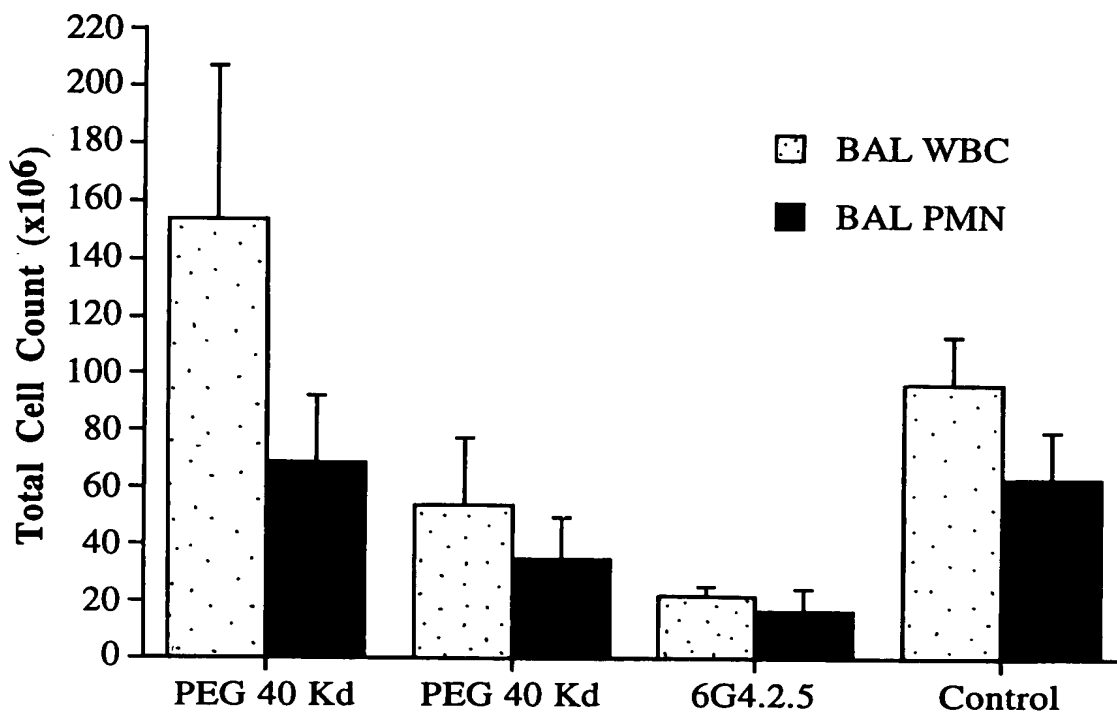


FIG. 68



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

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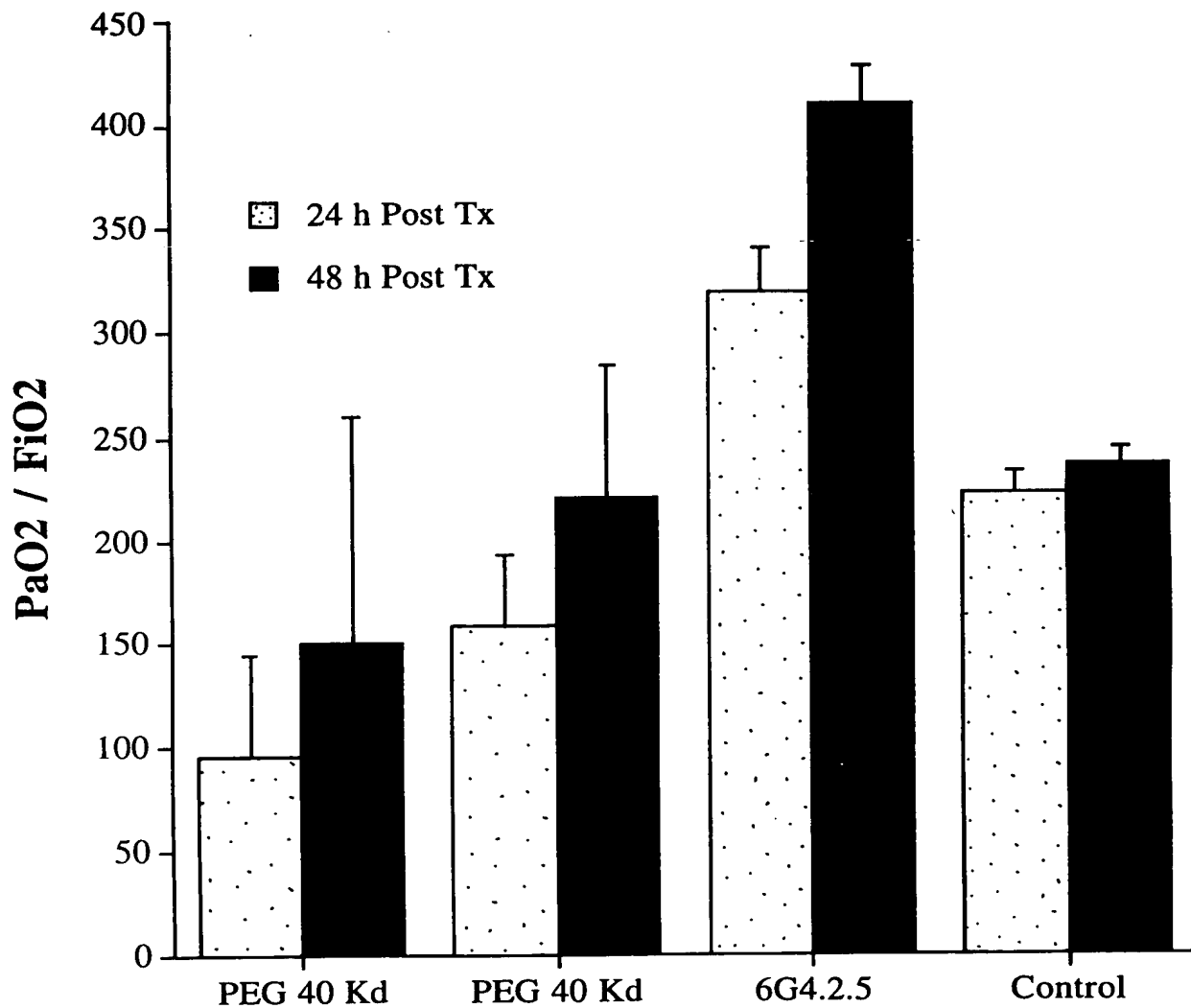


FIG. 69



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

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Oxygenation in 100% O₂ @24 h Post Anti-IL8 Tx

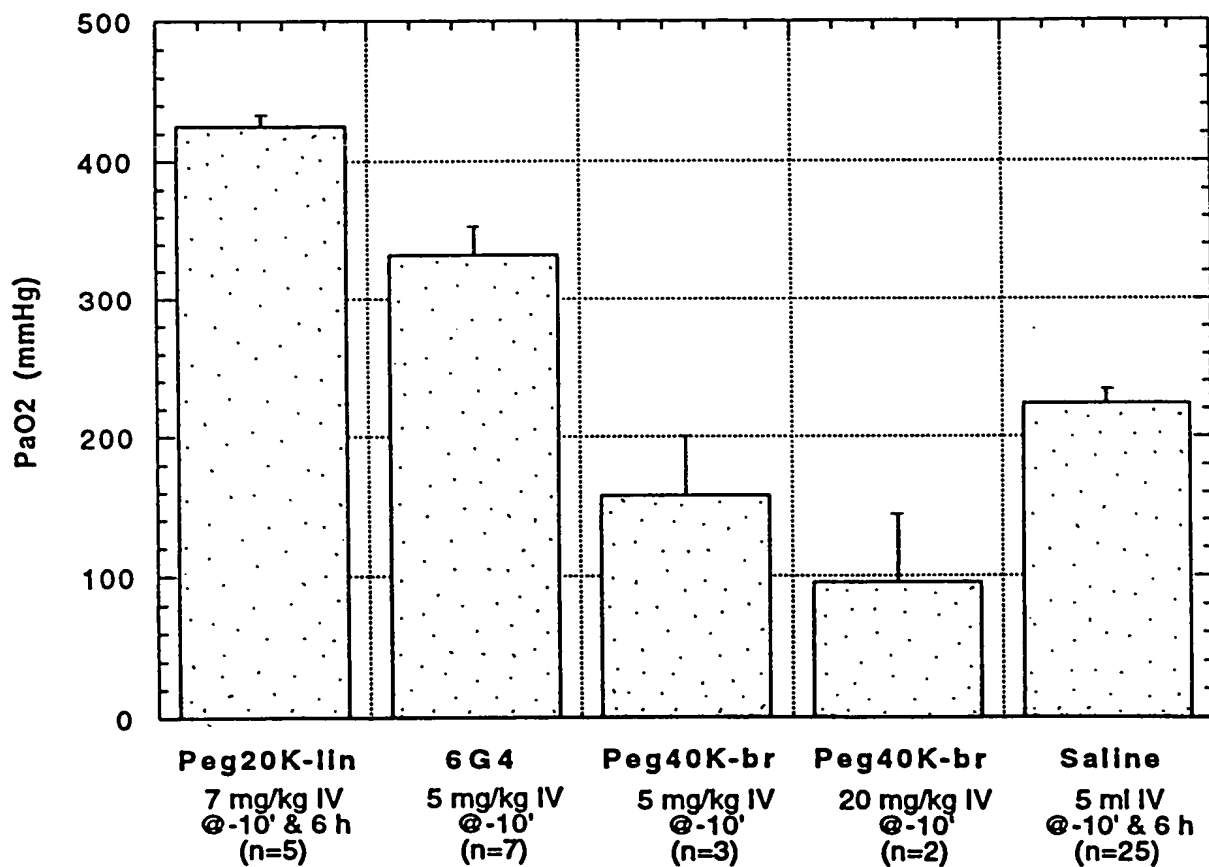


FIG. 70A



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

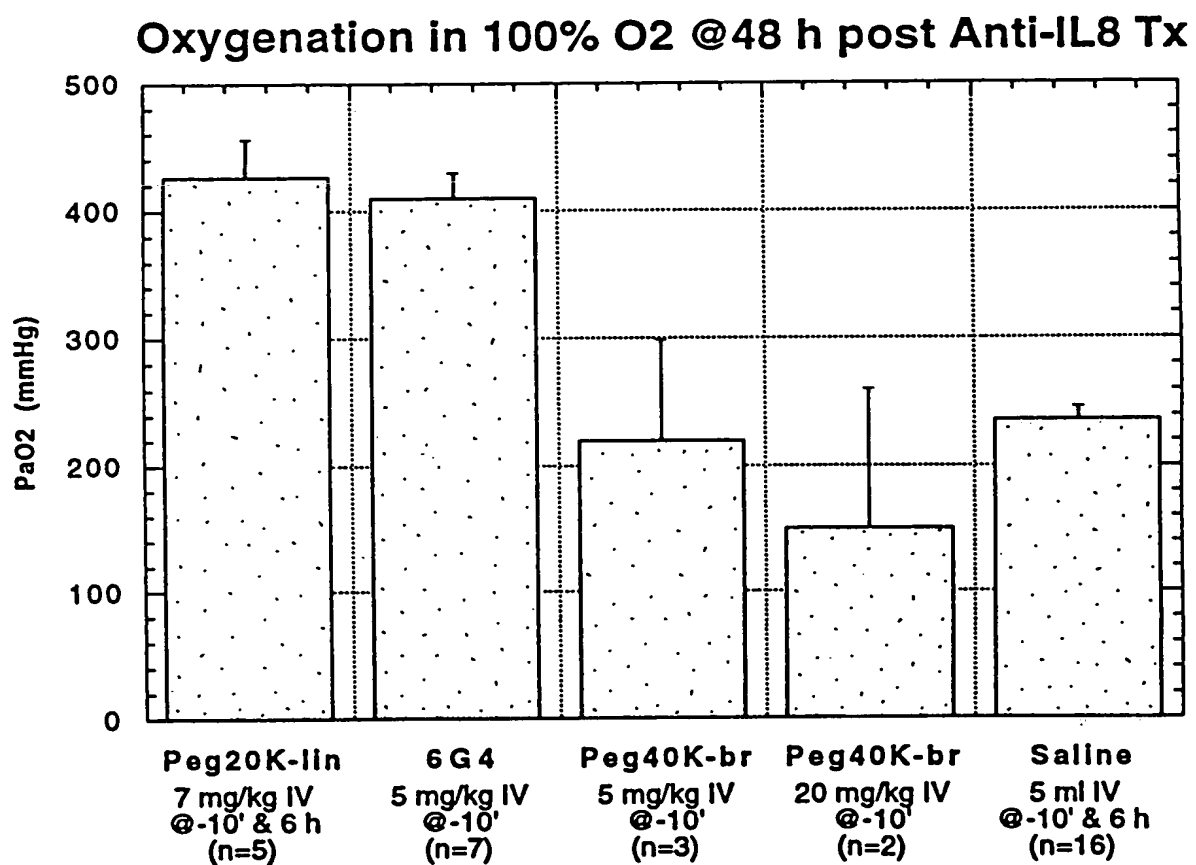


FIG. 70B



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

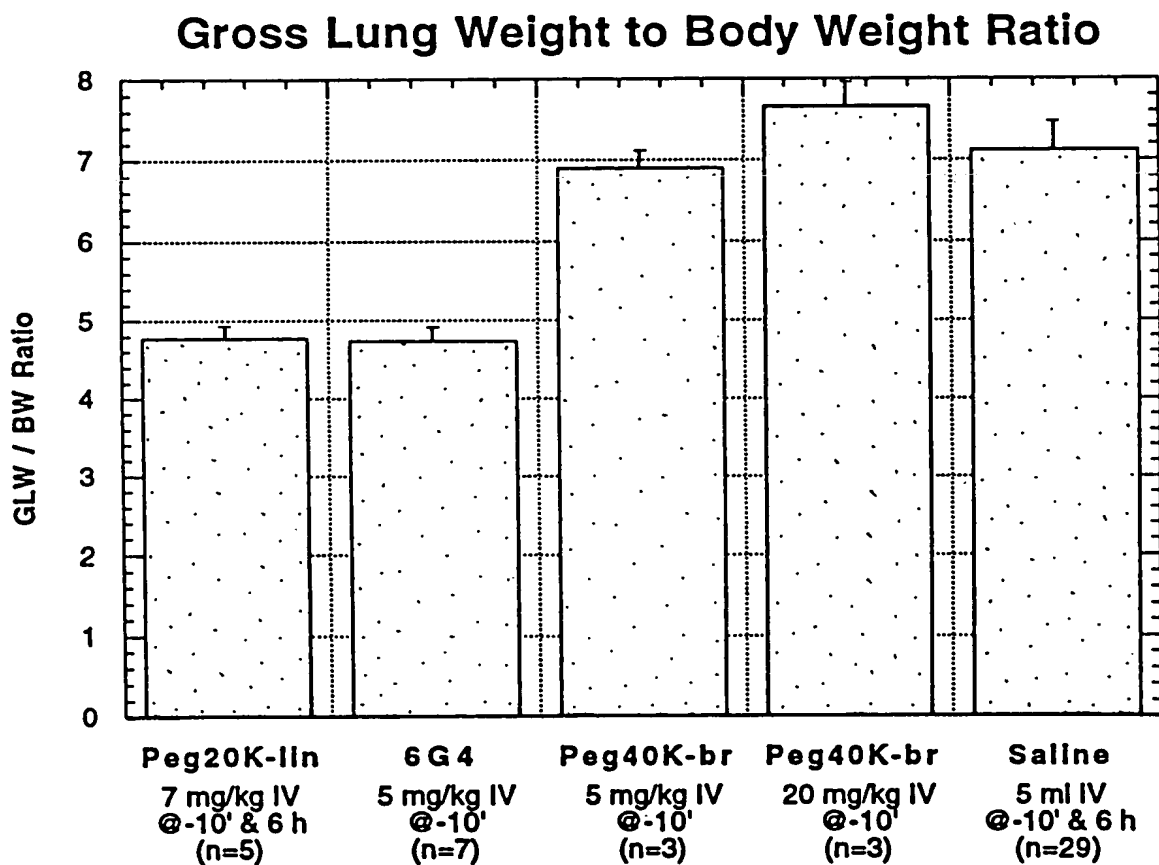


FIG. 70C



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

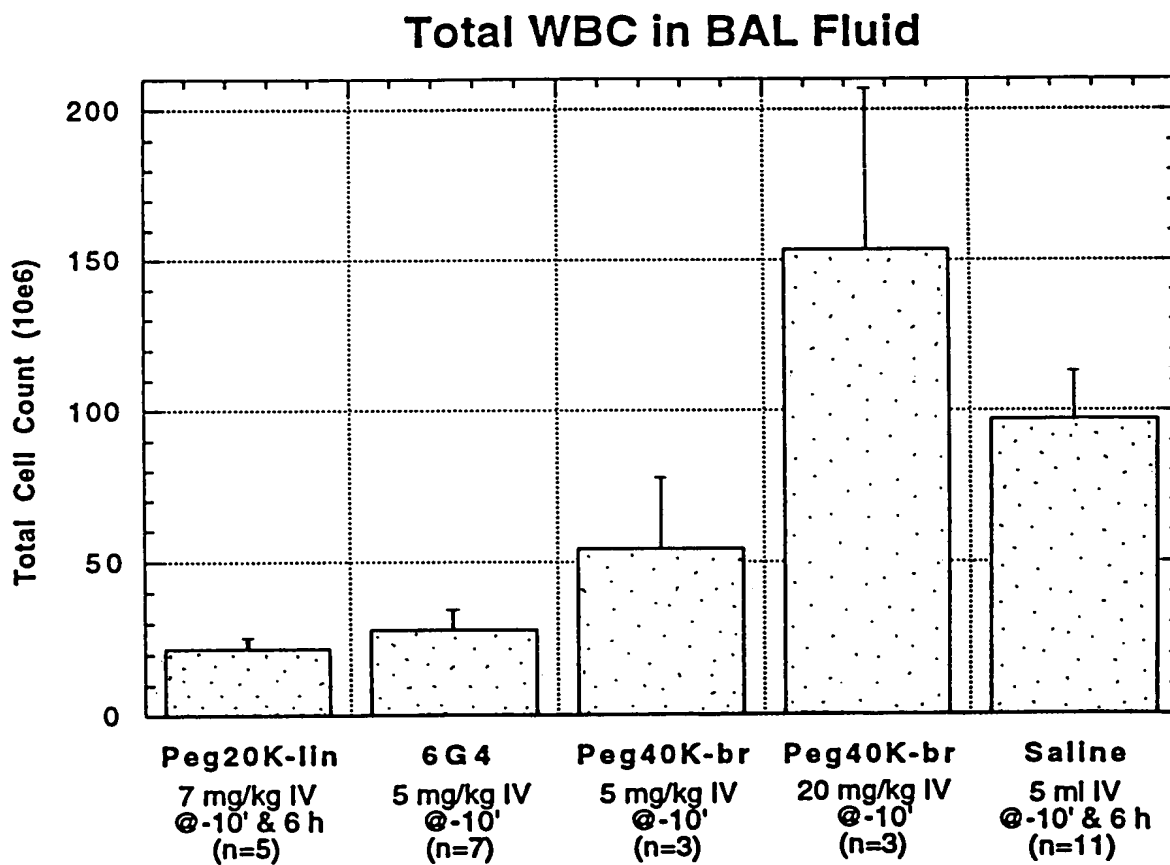


FIG. 70D



ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED
ANTI-IL-8 MONOCLONAL ANTIBODIES

Hsei et al.

Appl. No.: 09/234,182 Atty Docket: GENENT.093A

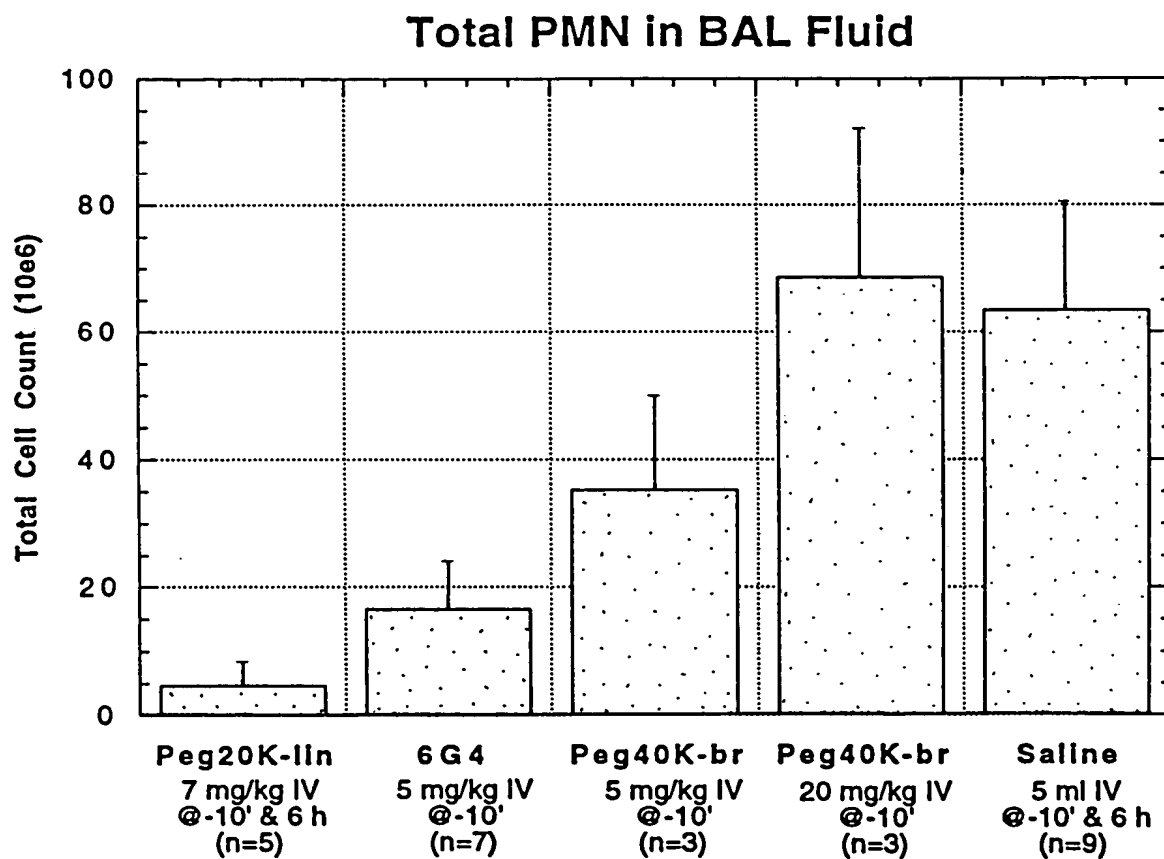
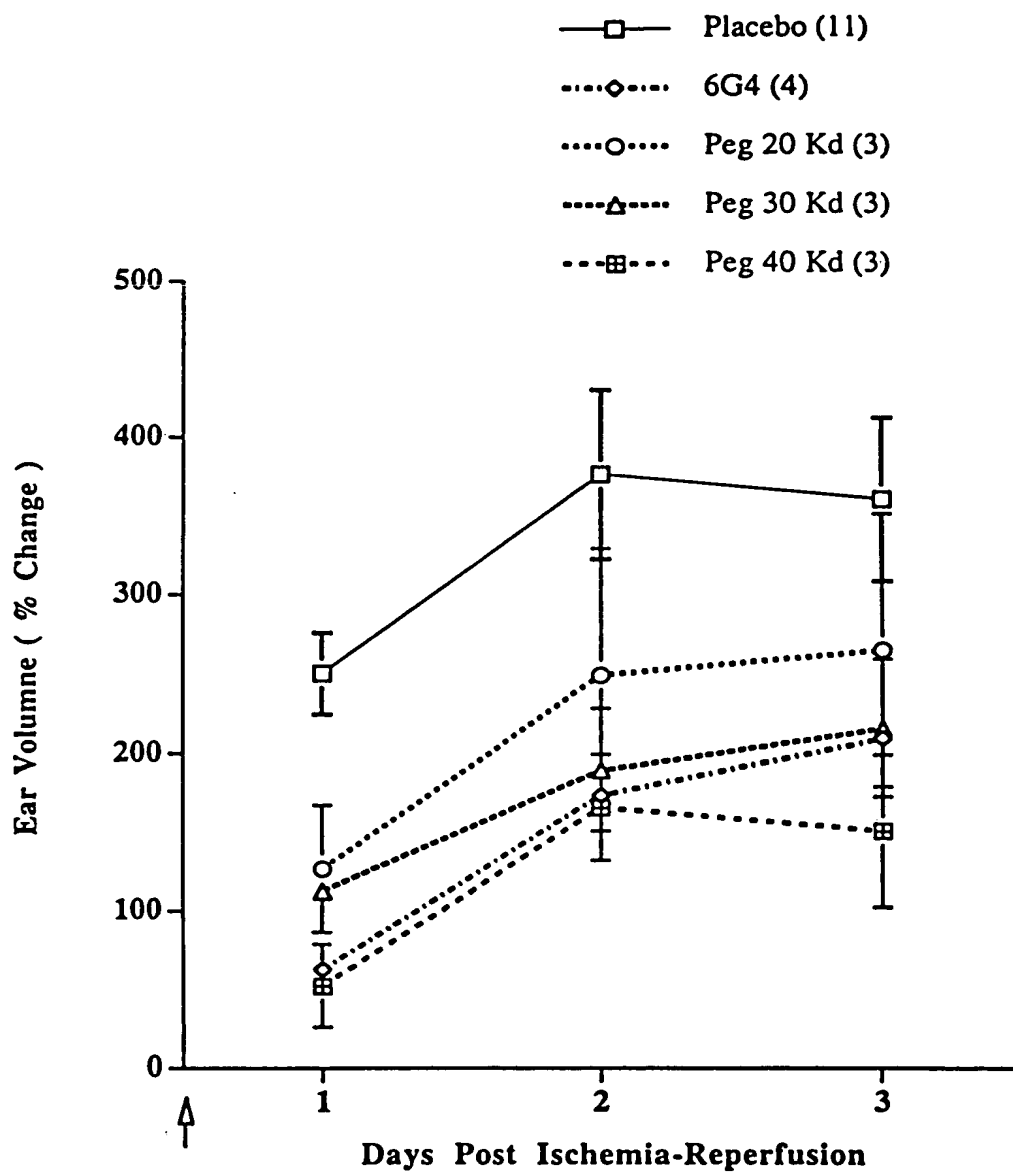


FIG. 70E



The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations :
Single Dose (5 mg/kg)
administered IV at time
of reperfusion

FIG. 71